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Korelacja badań audiologicznych, otoneurologicznych oraz obrazu klinicznego z zaawansowaniem wodniaka endolimfatycznego w badaniu rezonansu magnetycznego u pacjentów z chorobą Ménière'a

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu
w dyscyplinie nauki medyczne

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Wykaz stosowanych skrótów

MD	choroba Ménière'a (ang. *Ménière's disease*)
AAO-HNS	Amerykańska Akademia Otorynolaryngologii, Chirurgii Głowy i Szyi (ang. *American Academy of Otorhinolaryngology, Head and Neck Surgery*)
EH	wodniak endolimfatyczny (ang. *endolymphatic hydrops*)
MRI	badanie rezonansu magnetycznego (ang. *magnetic resonance imaging*)
PTA	średni próg słyszenia (ang. *pure tone average*)
ABR	słuchowe potencjały wywołane pnia mózgu (ang. *auditory brainstem response*)
TT-ECochG	elektrokochleografia transtympanalna (ang. *transtympanic electrocochleography*)
SP	potencjał sumacyjny (ang. *summating potential*)
AP	potencjał czynnościowy (ang. *acting potential*)
VNG	wideonystagmografia (ang. *videonystagmography*)

Streszczenie w języku polskim

Wstęp

Choroba Ménière'a charakteryzuje się występowaniem napadowych wirowych zawrotów głowy, którym towarzyszy szum uszny i/lub uczucie pełności w uchu oraz fluktuacyjny niedosłuch odbiorczy. Pomimo wielu badań etiologia choroby pozostaje nieznana, jednak uważa się, że u podłoża schorzenia leży poszerzenie przestrzeni endolimfatycznych ucha wewnętrznego zwane wodniakiem śródchłonki. Rozwój techniki badania rezonansu magnetycznego (MR) w ostatnich latach umożliwił przyżyciowe obrazowanie wodniaka endolimfatycznego u pacjentów z objawami choroby Ménière'a. Ocena wodniaka śródchłonki w badaniu MR jest zagadnieniem stosunkowo nowym na świecie (publikacje na ten temat zaczęły pojawiać się niedawno), a w Polsce jeszcze nie publikowanym.

Publikacja 1

Jasińska A, Lachowska M, Wnuk E, Niemczyk K. Magnetic resonance imaging of the inner ear in the diagnostics of Ménière's disease. Otorynolaryngologia Polska 2021:75(2):1-8. DOI: 10.5604/01.3001.0014.6176

Prezentowany artykuł w szczegółowy sposób przybliża metody oceny wodniaka śródchłonki w badaniu MR po dożylnym podaniu kontrastu stanowiąc dokładny przegląd literatury dotyczącej tematu wsparty naszym doświadczeniem i rycinami prezentującymi skany z badania MR obrazujące opisywane zmiany w ślimaku i przedsionku wykonane u naszych pacjentów w ramach niniejszej pracy doktorskiej. Obecnie najpowszechniejszą metodą obrazowania przestrzeni płynowych ucha wewnętrznego jest technika wymagająca wcześniejszego użycia środka kontrastowego podanego drogą transtympanalną lub dożylną. Wodniaka endolimfatycznego stwierdza się w przypadku poszerzenia przestrzeni endolimfatycznych, które widoczne są jako ubytki zakontrastowania na tle wzmacniającej się perylimfy. Wśród stosowanych obecnie skal do oceny zaawansowania wodniaka, możemy wyróżnić klasyfikacje opisowe, półilościowe oraz objętościowe. Badanie MR ucha wewnętrznego pozwala na diagnostykę pacjentów z niepełnym obrazem klinicznym, w którym dominują objawy audiologiczne takie jak szumy uszne czy uczucie pełności w uchu. Podczas leczenia, kontrolne badania MR pozwalają na ocenę skuteczności poszczególnych metod terapii pod kątem zaawansowania zmian w uchu wewnętrznym.

Publikacja 2

Jasińska A, Wnuk E, Pierchała K, Niemczyk K. Wodniak śródchłonki potwierdzony przy użyciu 3-teslowego skanera MR u pacjentów z obrazem klinicznym choroby Ménière'a. Polski Przegląd Otorynolaryngologiczny 2019;8(3):20-23.

W pracy przedstawiono opis dwóch przypadków wodniaka śródchłonki potwierdzonego w badaniu MR. W publikacji opisano technikę badania MR ucha wewnętrznego oraz skalę oceny zaawansowania wodniaka zaproponowaną przez Barath i wsp. Zaprezentowano dwa przypadki różniące się czasem trwania i obrazem klinicznym choroby Ménière'a, u których zobrazowano poszerzenie przestrzeni endolimfatycznych przy użyciu badania MR.

Publikacja 3

Jasińska A, Lachowska M, Wnuk E, Pierchała K, Rowiński O, Niemczyk K. Correlation between magnetic resonance imaging classification of endolymphatic hydrops and clinical manifestations and audiovestibular test results in patients with definite Ménière's disease. Auris Nasus Larynx, Ahead of print, DOI: 10.1016/j.anl.2021.03.027

Do badania włączono 38 pacjentów z jednostronną, zdefiniowaną klinicznie chorobą Ménière'a. Zaawansowanie wodniaka śródchłonki w MR zostało ocenione w oparciu o skalę opisaną przez Barath i wsp. oraz jej zmodyfikowaną wersję zaproponowaną przez Bernaerts i wsp. Celem badania było określenie korelacji pomiędzy zaawansowaniem wodniaka śródchłonki w badaniu MR a wynikami badań audiologicznych i otoneurologicznych oraz obrazem klinicznym. Analizując MR ucha wewnętrznego przy pomocy skali zaproponowanej przez Barath i wsp., wodniak endolimfatyczny w ślimaku stwierdzony został w 81.6% przypadków, natomiast w przedsionku w 63.2%. Po uwzględnieniu modyfikacji skali zaproponowanej przez Bernaerts i wsp., czułość badania wzrosła do 94.74%. Na podstawie przeprowadzonych badań można zaobserwować, że wodniak przedsionka obejmujący łagiewkę występował jedynie u pacjentów z poszerzonym przewodem ślimaka oraz powiększeniem woreczka. Stopień zaawansowania wodniaka w MR nie wykazywał korelacji z czasem trwania choroby oraz nasileniem głównych dolegliwości. Analizując związek pomiędzy stopniem niedosłuchu a wynikami MR wykazano istotną korelację pomiędzy średnim progiem słyszenia a zaawansowaniem wodniaka przedsionka ocenianego w skali zaproponowanej przez Bernaerts i wsp.

Podsumowanie

Przedstawione wyniki badań własnych dowodzą, że MR z kontrastem jest cennym badaniem w diagnostyce choroby Ménière'a i stwarza możliwość potwierdzenia obecności wodniaka śródchłonki za życia pacjenta. Wykazano istotne statystyczne różnice w czułości wykrywania wodniaka śródchłonki w MR pomiędzy skalą zaproponowaną przez Barath i wsp. oraz jej modyfikacją wprowadzoną przez Bernaerts i wsp. Wyniki przeprowadzonych badań pozwalają zauważyć korelacje pomiędzy stopniem zaawansowania wodniaka a wynikami badań dodatkowych.

Streszczenie w języku angielskim

Correlation between magnetic resonance imaging classification of endolymphatic hydrops and clinical manifestations and audiovestibular test results in patients with Ménière's disease

Introduction

Ménière's disease is a chronic inner ear disorder characterized by vertigo episodes with fluctuating low-frequency hearing loss, tinnitus, and aural fullness. Its etiology remains unknown, but the endolymphatic hydrops is considered underlying pathology. Due to the recent development of magnetic resonance imaging (MRI), visualization of enlarged endolymphatic space in patients with Ménière's disease symptoms is possible. MRI assessment of the endolymphatic hydrops is relatively new (publications on this subject have started appearing recently) and not yet published in Poland.

Manuscript #1

Jasińska A, Lachowska M, Wnuk E, Niemczyk K. Magnetic resonance imaging of the inner ear in the diagnostics of Ménière's disease. Otorynolaryngol Pol 2021:75(2):1-8. DOI: 10.5604/01.3001.0014.6176

The article presents in detail the methods of assessing the endolymphatic hydrops in MR after intravenous contrast administration. It provides a thorough literature review on the subject supported by our experience and figures presenting MR scans showing the described changes in the cochlea and vestibule in our patients. Over the last decade, several studies concerning MR imaging of the inner ear were completed using rearranged methods and protocols. Two different gadolinium-based contrast material delivery methods can be distinguished: intratympanic and intravenous injection. Several endolymphatic hydrops imaging evaluation methods already exist and can be divided into qualitative, semi-quantitative, and volumetric techniques. Inner ear MRI examinations facilitate diagnostics of patients with incomplete clinical presentation of Ménière's disease. In the treatment course, follow-up MRI scans enable assessing individual treatment modalities' efficacy in terms of the severity of lesions within the inner ear.

Manuscript #2

Jasińska A, Wnuk E, Pierchała K, Niemczyk K. Wodniak śródchłonki potwierdzony przy użyciu 3-teslowego skanera MR u pacjentów z obrazem klinicznym choroby Ménière'a. Polski Przegląd Otorynolaryngologiczny 2019;8(3):20-23.

The manuscript presents a study of two patients with endolymphatic hydrops confirmed by MRI. MRI visualization technique of the inner ear with a presentation of assessment scale of endolymphatic hydrops in the affected ears showing widening of the endolymphatic spaces proposed by Barath et al. are presented and illustrated by a detailed description of two Ménière's disease cases with different disease duration and clinical manifestations.

Manuscript #3

Jasińska A, Lachowska M, Wnuk E, Pierchała K, Rowiński O, Niemczyk K. Correlation between magnetic resonance imaging classification of endolymphatic hydrops and clinical manifestations and audiovestibular test results in patients with definite Ménière's disease. Auris Nasus Larynx, Ahead of print, DOI: 10.1016/j.anl.2021.03.027

Thirty-eight patients with unilateral definite Ménière's disease were enrolled in this study. The severity of the main clinical symptoms, audiovestibular tests, and MRI were evaluated. Endolymphatic space dilatation was assessed using Barath and Bernaerts grading systems. The purpose was to evaluate MRI classification of endolymphatic hydrops with clinical features, audiological and vestibular tests in patients with Ménière's disease. Using the Barath system, cochlear hydrops was visualized in 81.6% of affected ears, while vestibular in 63.2%. Sensitivity increased to 94.7% in the case of vestibular hydrops using Bernaerts' modification. Vestibular hydrops involving the utricle was present only among patients with cochlear and saccular endolymphatic space dilatation. The grade of the hydrops correlated neither with the duration of Ménière's disease nor with the severity of main clinical symptoms. There was a significant relationship between the hearing level threshold and the vestibular hydrops degree in the Bernaerts scale found, which confirms endolymphatic space dilatation's role in the hearing loss in ears affected by Ménière's disease.

Conclusions

Our studies proved MRI to be a sensitive diagnostic tool in Ménière's disease. Assessing vestibular hydrops in MRI, the Bernaerts scale was found to be significantly more sensitive than the Barath scale. Several correlations between the MRI visualization of endolymphatic hydrops and clinical data were found.

Korelacja badań audiologicznych, otoneurologicznych oraz obrazu klinicznego z zaawansowaniem wodniaka endolimfatycznego w badaniu rezonansu magnetycznego u pacjentów z chorobą Ménière'a

Wstęp

Choroba Ménière'a charakteryzuje się występowaniem ataków wirowych zawrotów głowy z towarzyszącymi nudnościami i wymiotami, szumem usznym, uczuciem pełności w uchu oraz fluktuacyjnym niedosłuchem. Rozpoznanie stawiane jest na podstawie typowego obrazu klinicznego oraz niedosłuchu odbiorczego udokumentowanego w badaniu audiometrii tonalnej. W diagnostyce wykonywane są także dodatkowe badania audiologiczne i otoneurologiczne mające na celu ocenę funkcjonowania narządu słuchu i równowagi.

Pomimo wielu badań przyczyna choroby Ménière'a pozostaje nieznana, a w patogenezie brane są pod uwagę czynniki genetyczne, infekcyjne, autoimmunologiczne oraz zaburzenia krążenia w obrębie ucha wewnętrznego. Za morfologiczne podłoże choroby Ménière'a uznaje się poszerzenie przestrzeni endolimfatycznych określane mianem wodniaka śródchłonki. Do niedawna potwierdzenie choroby wymagało badania histopatologicznego post-mortem. Rozwój techniki badania rezonansu magnetycznego (MR) w ostatnich latach umożliwił obrazowanie przestrzeni płynowych ucha wewnętrznego, a tym samym przyżyciowe potwierdzenie wodniaka śródchłonki u pacjentów z objawami choroby Ménière'a. Wizualizacja ucha wewnętrznego dokonywana jest po zastosowaniu kontrastu gadolinowego, który selektywnie przenika do przestrzeni perylimfatycznej, podczas gdy endolimfa pozostaje widoczna jako ubytki w zakontrastowaniu. Od czasu pierwszych doniesień na temat zastosowania MR w diagnostyce choroby Ménière'a, powstały różnorodne skale oceniające zaawansowanie wodniaka śródchłonki. Trzystopniowa skala zaproponowana przez Barath i wsp. w 2014 r. ocenia poszerzenie przestrzeni endolimfatycznych oddzielnie w ślimaku i w przedsionku. Wodniak ślimaka jest oceniany w oparciu o stopień przemieszczenia błony Reissnera wskutek poszerzenia wypełnionego endolimfą przewodu ślimaka. W przypadku przedsionka oceny zaawansowania wodniaka dokonuje się w oparciu o powiększenie struktur wypełnionych endolimfą tj. woreczka oraz łagiewki. W 2019 r. Bernaerts i wsp. dokonali modyfikacji skali wodniaka przedsionka dodając początkowe stadium, w którym ma miejsce izolowane powiększenie woreczka.

Prezentowany cykl trzech artykułów stanowiących moją rozprawę doktorską dotyczy zastosowania badania MR ucha wewnętrznego w diagnostyce choroby Ménière'a oraz korelacji zaawansowania wodniaka śródchłonki z badaniami audiologicznymi, otoneurologicznymi oraz obrazem klinicznym choroby Ménière'a. Ocena wodniaka śródchłonki w badaniu MR jest

zagadnieniem stosunkowo nowym na świecie, a publikacje na ten temat zaczęły pojawiać się niedawno. W literaturze polskiej tematyka ta jeszcze nie była poruszana, a prezentowane prace stanowiące moją rozprawę doktorską są pierwszymi w naszym kraju dotyczącymi omawianego zagadnienia.

Pierwsza praca prezentowanego cyklu *(**Jasińska A**, Lachowska M, Wnuk E, Niemczyk K. Magnetic resonance imaging of the inner ear in the diagnostics of Ménière's disease. Otorynolaryngologia Polska 2021:75(2):1-8. DOI: 10.5604/01.3001.0014.6176)* stanowi pierwszą w polskiej literaturze publikację omawiającą zagadnienie zastosowania MR w diagnostyce choroby Ménière'a. Artykuł w szczegółowy sposób przybliża metody oceny wodniaka śródchłonki w badaniu MR po dożylnym podaniu kontrastu stanowiąc dokładny przegląd literatury dotyczącej tematu wsparty naszym doświadczeniem i rycinami prezentującymi skany z badania MR obrazujące opisywane zmiany w ślimaku i przedsionku wykonane u naszych pacjentów w ramach niniejszej pracy doktorskiej. Przedstawiono metodologię badania MR ucha wewnętrznego, porównano różnorodne skale służące do oceny zaawansowania wodniaka śródchłonki, które zaprezentowano na konkretnych przykładach. Ponadto omówiono zastosowanie MR w diagnostyce pacjentów o niepełnym i atypowym obrazie klinicznym choroby oraz ocenę zaawansowania wodniaka śródchłonki jako metodę pomocną w monitorowaniu efektów leczenia zachowawczego i chirurgicznego tej choroby.

Drugą pracę prezentowanego cyklu (***Jasińska** A, Wnuk E, Pierchała K, Niemczyk K. Wodniak śródchłonki potwierdzony przy użyciu 3-teslowego skanera MR u pacjentów z obrazem klinicznym choroby Ménière'a. Polski Przegląd Otorynolaryngologiczny 2019;8(3):20-23*) stanowi opis dwóch przypadków wraz z przeglądem literatury. W publikacji opisano zastosowaną metodę badania MRI ucha wewnętrznego oraz skalę oceny zaawansowania wodniaka zaproponowaną przez Barath i wsp. Zaprezentowano dwóch pacjentów z chorobą Ménière'a o różnym czasie trwania oraz przebiegu klinicznym, u których przy pomocy MR potwierdzono obecność wodniaka śródchłonki. Praca stanowi pierwsze w polskiej literaturze doniesienie dotyczące potwierdzenia w badaniu obrazowym poszerzenia przestrzeni endolimfatycznych u pacjentów z objawami choroby Ménière'a.

Trzecia praca prezentowanego cyklu (***Jasińska A**, Lachowska M, Wnuk E, Pierchała K, Rowiński O, Niemczyk K. Correlation between magnetic resonance imaging classification of endolymphatic hydrops and clinical manifestations and audiovestibular test results in patients with definite Ménière's disease. Auris Nasus Larynx, Ahead of print. DOI: 10.1016/j.anl.2021.03.027*) to artykuł oryginalny, w którym dokonano szczegółowej analizy korelacji zaawansowania wodniaka endolimfatycznego w badaniu MR z wynikami badań dodatkowych oraz obrazem klinicznym w grupie 38 chorych ze zdefiniowaną, jednostronną

chorobą Ménière'a. Zaawansowanie poszerzenia przestrzeni endolimfatycznych w badaniu obrazowym oceniono przy pomocy dwóch skal - opisanej przez Barath i wsp. oraz jej modyfikacji zaproponowanej przez Bernaerts i wsp. Pomiędzy skalami stwierdzono istotne statystycznie różnice dotyczące czułości w wykrywaniu wodniaka śródchłonki. Analizowano także korelacje pomiędzy zaawansowaniem wodniaka w obrazach MR a wynikami badań audiologicznych i otoneurologicznych, w których stwierdzono istotne różnice w zależności o d skali użytej do oceny MR.

Z uwagi na rozwój technik diagnostyki obrazowej, audiologicznej oraz otoneurologicznej w ostatnim czasie, pojawiła się potrzeba korelowania zaawansowania wodniaka śródchłonki w badaniu rezonansu magnetycznego z wynikami badań dodatkowych oraz obrazem klinicznym choroby Ménière'a. Badanie rezonansu magnetycznego w chorobie Ménière'a może być pomocne w diagnozowaniu tej choroby i może pomóc w lepszym zrozumieniu jej patofizjologii. Badanie to wzbogaca wiedzę i poszerza diagnostykę tym samym wspierają opiekę zdrowotną nad pacjentami z chorobą Ménière'a.

Założenia i cel pracy

1. Analiza zaawansowania wodniaka śródchłonki w badaniu rezonansu magnetycznego u pacjentów z chorobą Ménière'a przy użyciu skali opisanej przez Barath i wsp. oraz jej modyfikacji zaproponowanej przez Bernaerts i wsp.
2. Ocena korelacji zaawansowania wodniaka śródchłonki w badaniu rezonansu magnetycznego z kontrastem z wynikami badań audiologicznych i badań układu równowagi oraz nasileniem objawów u pacjentów ze zdefiniowaną z chorobą Ménière'a.

INDEX COPERNICUS INTERNATIONAL

ORIGINAL ARTICLE

Magnetic resonance imaging of the inner ear in the diagnostics of Ménière's disease

Authors' Contribution:
A – Study Design
B – Data Collection
C – Statistical Analysis
D – Data Interpretation
E – Manuscript Preparation
F – Literature Search
G – Funds Collection

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ABSTRACT: Ménière's disease is characterized by sudden episodes of vertigo accompanied by tinnitus and/or feeling of fullness in the ear as well as fluctuating sensorineural hearing loss. Despite numerous studies, the etiology of this disease remains unknown. However, the enlargement of the inner ear's endolymphatic spaces, referred to as endolymphatic hydrops, is considered the underlying condition. Thanks to recent advances in magnetic resonance (MR) technology, it is now possible to obtain in vivo imaging of endolymphatic hydrops in patients presenting with Ménière's disease symptoms. Visualization of the inner ear fluid compartments is achieved after gadolinium contrast is administered into the tympanic cavity or via the intravenous route. Evaluation of endolymphatic hydrops is possible as the contrast agent selectively penetrates the perilymph, and endolymph is visualized as contrast defects. The currently used radiological hydrops grading systems include qualitative, semi-quantitative, and volumetric scales. The methods are subject to ongoing modifications to increase their sensitivity and specificity. Numerous studies describe correlations between clinical symptoms and audiological and otoneurological examination results with the endolymphatic hydrops grade. MRI is also applicable in patients' diagnostics with an incomplete or atypical course of the Ménière's disease. In the course of the treatment, follow-up MRI scans enable assessing individual treatment modalities' efficacy in terms of the severity of lesions and the further course of the disease within the inner ear.

KEYWORDS: endolymphatic hydrops, hearing loss, magnetic resonance, Ménière's disease, vertigo

ABBREVIATIONS

AAO-HNS – American Academy of Otolaryngology-Head and Neck Surgery
AP – action potential amplitude
CVEMP – cervical vestibular evoked myogenic potentials
MR – magnetic resonance
OVEMP – ocular vestibular evoked myogenic potentials
SP – summating potential amplitude
SURI – saccule to urticle ratio inversion
VNG – videonystagmography

INTRODUCTION

Ménière's disease's clinical presentation consists of vertigo episodes with nausea and vomiting, fluctuating low-frequency hearing loss, tinnitus, and/or feeling of congestion within the ear [1–3]. The natural history of the disease varies between individuals and includes periods of exacerbations and spontaneous remission. Ménière's disease affects patients of all ages, with incidence peaking in the fifth and the sixth decade of life [4]. In most cases, symptoms are unilateral at the time of diagnosis. Still, the risk of symptoms within the contralateral ear increases with the disease's duration and affects 2–73% of patients, according to literature sources [5–9]. Ménière's disease's etiology remains unknown, with autoimmune processes, infections, allergies, cardiovascular disorders, chronic middle and inner ear diseases being proposed as potential causes [5, 10–12]. In 5 to 15% of cases, the disease is inherited within families following an autosomal dominant pattern with incomplete penetrance [13].

Ménière's disease has been a subject of interest for researchers for more than 150 years since Prosper Ménière first linked the presence of vertigo to a pathology of the inner ear [14]. More than 70 years later, Hallpike and Cairns [15] and Yamakawa [16] analyzed the temporal bones of patients presenting with symptoms corresponding to Ménière's disease to observe the enlargement of endolymphatic spaces within the inner ears of these patients. This presentation was subsequently termed the endolymphatic hydrops.

For many years, endolymphatic hydrops has been considered the morphological origin of Ménière's disease symptoms, although confirmation was possible only in post-mortem histopathological examinations [1].

The introduction of MRI offered new possibilities for the diagnostics of endolymphatic hydrops. Previously, MRI was used in patients presenting with Ménière's disease symptoms to exclude other vertigo causes, such as nerve VIII tumors. In 2007, Nakashima et al. [17] were the first to observe that gadolinium contrast, when introduced into the tympanic membrane, is accumulated in perilymphatic spaces. A similar effect was observed later by Naganawa et al. [18] following intravenous administration of a double dose of the contrast agent.

Tab. I. Semi-quantitative MR-based scale for endolymphatic hydrops grading according to Nakashima et al. [19] and Naganawa et al. [18].

ENDOLYMPHATIC HYDROPS GRADING SCALE ACCORDING TO NAKASHIMA AND NAGANAWA	
Cochlea	
Healthy condition	No cochlear duct enlargement
Moderate grade	Cochlear duct enlargement Cochlear duct narrower than the scala vestibuli
Significant grade	Enlarged cochlear duct extending into the scala vestibuli
Vestibule **(Endolymphatic space *vs* vestibular fluid space area ratio)**	
Healthy condition	≤33.3%
Moderate grade	>33.3% but ≤50%
Significant grade	>50%

Tab. II. Morphological assessment of endolymphatic hydrops in magnetic resonance (MR) imaging scans based on the SURI value proposed by Attyé et al. [21]. *SURI – saccule to urticle ratio inversion.

MORPHOLOGICAL ASSESSMENT OF ENDOLYMPHATIC HYDROPS IN MRI SCANS AS PROPOSED BY ATTYÉ ET AL.		
Hydrops grade	**Saccule**	**SURI***
Grade 0	not enlarged	<1
Grade 1	enlarged	≥1
Grade 2	invisible	not applicable

Tab. III. Descriptive MR-based scale for endolymphatic hydrops grading according to Barath et al. [22] as modified by Bernaerts et al. [23].

COCHLEA – THE ASSESSMENT OF ENDOLYMPHATIC HYDROPS IN MRI SCANS		
Barath scale **(identical to Bernaerts scale)**		**Hydrops presentation in MRI**
Healthy condition		No cochlear duct enlargement
Grade I		Partial enlargement of the cochlear duct, visible obstruction of scala vestibuli
Grade II		Enlarged cochlear duct extending into the vestibular duct
Vestibule – the assessment of endolymphatic hydrops in MRI scans		
Barath scale	**Bernaerts scale**	**Hydrops presentation in MRI**
Healthy condition	**Healthy condition**	Saccule and utricle not enlarged, saccule smaller than the utricle
	Grade I	Saccule larger than the utricle, boundary between the two is maintained
Grade I	**Grade II**	Enlargement and overlapping of saccule and utricle, peripheral contrast enhancement
Grade II	**Grade III**	significant enlargement of saccule and utricle, no contrast enhancement within the vestibule

MRI PROTOCOL IN THE DIAGNOSTICS OF ENDOLYMPHATIC HYDROPS

The most common modality for the imaging of inner ear fluid compartments consists of T2-3D fluid-attenuated inversion recovery (FLAIR) images requiring previous administration of a contrast agent. The evaluation is based on the finding that the contrast agent selectively penetrates the perilymph while the endolymph remains uncontrasted. Gadolinium contrasts may be administered via the transtympanic [17] and intravenous [18] routes. When administered via the transtympanic route, the contrast agent penetrates the inner ear in the round window and the oval window region and across the medial walls' continuity. It is estimated that the accumulation of gadolinium within the perilymphatic space takes approximately 24 hours. If a double dose of the gadolinium agent is administered intravenously, scans can be acquired as early as after 4 hours. Other benefits of intravenous contrast administration include assessing both inner ears simultaneously and avoiding the puncturing of the tympanic membrane.

METHODS FOR EVALUATION OF ENDOLYMPHATIC HYDROPS IN MAGNETIC RESONANCE SCANS

Endolymphatic hydrops is observed as enlargement of endolymphatic spaces presenting as contrast defects against contrast-enhanced perilymph. Since the first reports on MR's use in Ménière's disease's diagnostics, numerous authors have proposed various scales for endolymphatic hydrops grading. The currently used radiological hydrops grading systems include qualitative, semi-quantitative, and volumetric scales. The selected classifications are summarized in Tab. I.–III.

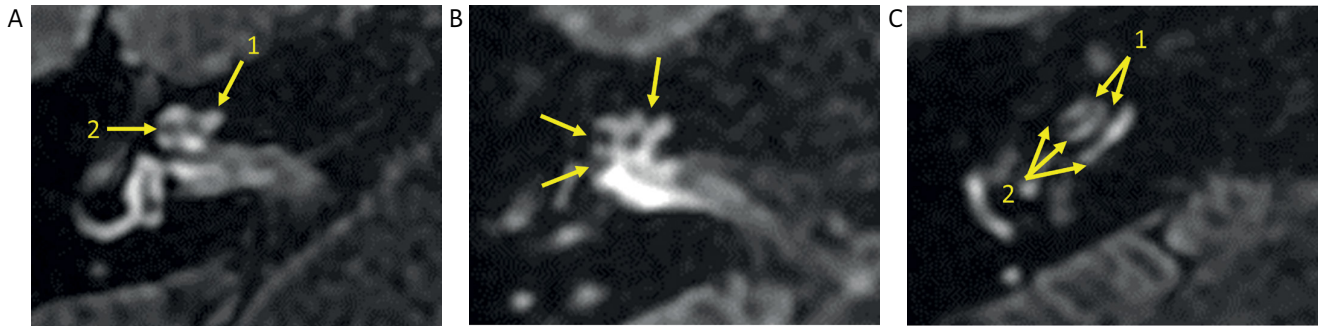

Fig. 1. MRI of the inner ear – a 3D-FLAIR T2-weighted sequence performed 4 hours after intravenous administration of a double dose of the contrast agent – assessment of the cochlear hydrops grade, according to Barath et al. [22] and Bernaerts et al. [23]. (A) The typical image of the cochlea without enlargement of endolymphatic spaces – arrow #1 points to contrast-enhanced scala vestibuli and scala tympani, arrow #2 points to the osseous spiral lamina and the narrow cochlear duct visible as a slight defect in contract enhancement; (B) grade I cochlear hydrops – arrows point to partial enlargement of the cochlear duct, obstruction of scala vestibuli is also visible; (C) grade II cochlear hydrops – arrows #1 point to the cochlear hydrops, significantly enlarged along the entire length and extending into the scala vestibuli area; arrows #2 point to the contrast-enhanced scala tympani.

The semi-quantitative scale described by Nakashima et al. [19] in 2009 (Tab. I.) is commonly used for the grading of endolymphatic hydrops visualized in MRI scans. For this purpose, a single cross-sectional image of the inner ear is analyzed. Within the cochlea, the assessment is based on the contrast defects within the scala vestibuli corresponding to the cochlear duct being enlarged due to the Reissner's membrane dislocation. Moderate-grade endolymphatic hydrops appears enlarged but still narrower than the scala vestibuli. Significant-grade endolymphatic hydrops is characterized by the cochlear duct being wider than the scala vestibuli. The assessment consists of comparing the contrast-defective area of endolymph to the total area or endo- and perilymph within the vestibule. Endolymph accounting for <33% of the vestibular area is considered normal, whereas moderate endolymphatic hydrops is diagnosed for endolymph accounting for 33–50% of the total area. When the non-enhanced area accounts for >50% of the total vestibular area, the endolymphatic hydrops is considered advanced.

In 2018, Conte et al. [20] published a review of studies using the grading scale proposed by Nakashima. Significant differences in sensitivity and specificity of endolymphatic hydrops detection were observed for the method used in 17 studies analyzed in the review. Patients with Ménière's disease symptoms presented with endolymphatic hydrops in 36–100% of symptomatic ears and 46% of asymptomatic ears. On the other hand, in healthy volunteers, cochlear duct enlargement was observed in 13–33% of subjects. Vestibular location of moderate-to-significant endolymphatic hydrops was reported for 94–100% of symptomatic ears in patients with Ménière's disease, albeit some studies reported its also being present in 53–100% of asymptomatic ears as well as in healthy subjects. Attyé et al. [21] analyzed results obtained for patients with Ménière's disease in 30 symptomatic ears and 30 healthy ears. They reported that endolymphatic hydrops was present within the cochlea and/or the vestibule in 100% of cases. For this reason, Attyé et al. [21] undertook a detailed analysis of vestibular MRI images. They proposed a new parameter, referred to as the saccule to utricle ratio inversion (SURI), determined using a single reference sagittal cross-section (Tab. II.). Under physiological conditions, the saccule is smaller than the utricle, and the SURI is < 1. The authors of the study found that 50% of Ménière's disease patients presented with SURI of ≥ 1, whereas elevated values of the parameter were absent from the control group (specificity of 100%).

As proposed by Barath et al. [22] in 2014, the three-grade scale evaluates the enlargement of endolymphatic spaces separately within the cochlea and the vestibule (Tab. III., Figs. 1. and 2.). For the cochlea, grade 0 corresponds to no cochlear enlargement, grade I corresponds to partial enlargement of the cochlear duct and visible obstruction of scala vestibuli. In contrast, grade II corresponds to Reissner's membrane's significant dislocation, making it impossible to visualize the perilymph within the scala vestibuli. Similarly, concerning the vestibule, grade 0 corresponds to no enlargement of the saccule or utricle, grade I corresponds to the enlargement and overlapping of the saccule and utricle with peripheral contrast enhancement. In contrast, grade II corresponds to no contrast enhancement being detected within the vestibule as its area is fully encompassed by endolymphatic space. The authors analyzed the results of the MRI scans in 53 patients with symptoms indicative of the Ménière's disease and found the presence of endolymphatic hydrops in 90% of symptomatic ears, with the sensitivity of the method being as high as 95% when only the group of patients with the definite disease was included in the analysis. Endolymphatic hydrops was also detected in 22% of asymptomatic, contralateral ears.

In 2019, Bernaerts et al. [23] modified Barath's scale by adding a „lower" grade I where the saccule is greater or equal in size to the utricle, but the boundary between the two is still visible (Tab. III., Figs. 1. and 2.). Thus, in the Bernaerts modification, the scale for the assessment of vestibular hydrops is four-grade. In addition, the authors compared the degree of contrast enhancement within the cochlea on the symptomatic side and the contralateral side. They reported an asymmetrical increase in contrast enhancement to be characteristic for symptomatic ears (specificity of 97.4%). The algorithm for the MRI assessments of the inner ear, as proposed in this study, assumes that the higher enhancement of the cochlea on the symptomatic side is equivalent to the presence of endolymphatic hydrops. The reported results suggest the involvement of the blood-perilymph barrier disorders in the pathogenesis of Ménière's disease.

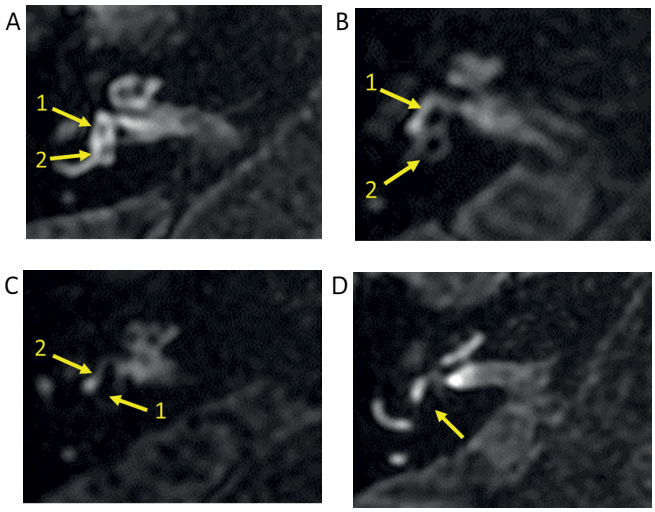

Fig. 2. MRI of the inner ear – a 3D-FLAIR T2-weighted sequence performed 4 hours after intravenous administration of a double dose of the contrast agent. Assessment of the vestibular hydrops grade according to Barath et al. [22] and including modification by Bernaerts et al. [23]. (A) normal vestibule – arrow #1 points to non-enlarged saccule and arrow #2 points to the utricle; the border between the two is maintained and visible; (B) vestibular hydrops of the lowest grade I according to the Bernaerts modification (within normal limits according to Barath) – the vestibule presents with enlarged saccule marked with arrow #1 and utricle marked with arrow #2; the boundary between the two is maintained, and marginal contrast enhancement of the vestibule can be seen; (C) vestibular hydrops of Barath grade I (Bernaerts grade II) – dilatation and overlapping of the saccule and the utricle is marked with arrow #1, peripheral contrast enhancement of the vestibule is marked with arrow #2; (D) vestibular hydrops of Barath grade II (Bernaerts grade III) – the significant enlargement and overlapping of the saccule and utricle is marked with the arrow; no contrast enhancement within the vestibule.

In 2019, Kahn et al. [24] proposed a classification based on the labyrinth's anatomical division where endolymphatic spaces of the saccule, utricle, and ampullae of semicircular canals were assessed separately. Saccular hydrops was detected in 91% of symptomatic ears; in 97% (i.e., all but one) cases in this group, saccular hydrops was accompanied by cochlear hydrops. Utricular hydrops was observed in 45% of symptomatic ears and always co-existed with the involvement of the saccule and the cochlea while the enlargement of semicircular canal ampullae was observed in as few as 8.5% of ears presenting with the symptoms of Ménière's disease; all these cases were associated with significant grades of cochlear, saccular, and utricular hydrops. The above results' analysis confirms the theory suggesting that hydrops develops initially within the cochlear duct to extend sequentially into the saccule, utricle, and semicircular canals [25].

Accurate assessment of the endolymphatic spaces in patients presenting with Ménière's disease symptoms can be achieved using volumetric methods. Gurkov et al. [26] assessed the percentage volumes of endolymphatic spaces within the cochlea and the vestibule of 16 patients. They observed a significant correlation between the enlargement of the cochlear tube and the degree of hearing impairment. The comparison of endolymphatic space volumes in patients with Ménière's disease and healthy volunteers carried out by Ito et al. [27] has proved important. It facilitated the outcomes being referred to the standard. The authors evaluated the total volume of spaces filled with endolymph and perilymph and determined the percentage share of endolymphatic space within the inner ear. In symptomatic ears, endolymph was found to occupy a significantly larger space than that in the ears of healthy volunteers and the asymptomatic ears of patients with Ménière's disease. Homann et al. [28] compared the volumetric method with the widespread semi-quantitative scale proposed by Nakashima et al. [29]. The authors also took note of the time needed to perform the analysis using both methods, stating that for the semi-quantitative assessment, a single evaluation lasted an average of 2.2 minutes, while 14.5 minutes were required for volumetric analysis. In this study, the volume of endolymphatic space in the group of 11 patients with Ménière's disease correlated with the degree of hearing loss; it was also significantly higher in patients with a longer history of the disease. The volumetric analysis results are consistent with the grade of endolymphatic hydrops as determined using the semi-quantitative scale, making it possible to consider the Nakashima and Naganawa method a reliable and rapid tool for the assessment of endolymphatic hydrops.

CORRELATION BETWEEN THE MR IMAGES OF ENDOLYMPHATIC HYDROPS AND THE CLINICAL PRESENTATION AND AUDIOLOGICAL AND OTONEUROLOGICAL EXAMINATION RESULTS

Ménière's disease's natural history is characterized by exacerbation periods and spontaneous remissions, the frequency of which varies from one case to another. The disease's fluctuating course is reflected in the inner ear imaging results showing variable grades of endolymphatic hydrops in repeated scans acquired in the same patient [29, 30].

Most of the studies carried out in recent years found no link between the endolymphatic hydrops grade and the disease's duration [24, 31, 32]. At the same time, only a few reported the existence of statistically significant correlations [23].

Numerous research papers describe the correlation between the pure-tone audiometry thresholds and the endolymphatic hydrops grade assessed from MR scans [24, 32–35]. This correlation may be crucial for a better understanding of processes developing within the inner ear and demonstrates the impact of endolymphatic space enlargement on hearing impairment.

The relationship between the endolymphatic hydrops grade and electrocochleography examination results was also analyzed. Seo et al. [34] divided their patients' population with established Ménière's disease into groups presenting with endolymphatic hydrops visualized in MRI scans vs. unremarkable MR images of the cochlea to observe a statistically significant difference in the summating to action potential ratios (SP/AP). Yamamoto et al. [36] carried out a similar study and reported the differences in the SP/AP values between groups of patients with different grades of endolymphatic hydrops. However, these differences were only statistically significant when patients with advanced cochlear hydrops were compared to patients with moderate hydrops or unremarkable MRI scans.

Examinations of the balance system and organs were analyzed in correlation with the images of corresponding structures. Caloric test responses obtained in the videonystagmographic (VNG) examination of the labyrinth was assessed in correlation with hydrops grades determined from MRI scans. Cho et al. [3] described the correlations between the reduction in labyrinthine excitability and endolymphatic space enlargement. They also observed that the caloric deficit was significantly higher in endolymphatic hydrops encompassing the horizontal semicircular canal's ampulla. Other studies revealed no significant correlation between the grade of endolymphatic hydrops and VNG results [32, 38]. Cervical and ocular vestibular evoked myogenic potentials (oVEMP and cVEMP) are used to assess the saccule's and the utricle's function, respectively [39–41]. Hence, the results of these examinations were examined for correlations with otolithic organ enlargement. Kahn et al. [24] and Seo et al. [34] failed to identify any significant correlation between the grade of endolymphatic hydrops within the saccule and the utricle and the oVEMP/cVEMP results. Gurkov et al. [33] reported a significant correlation between the grade of vestibular hydrops and reduced response amplitude in the cVEMP study.

MAGNETIC RESONANCE IN THE DIAGNOSTICS OF ATYPICAL COURSE OF MÉNIÈRE'S DISEASE

In addition to patients with the classical clinical presentation of Ménière disease, many patients with isolated symptoms such as periodic tinnitus, feeling of congestion within the ear, or recurring low-frequency sensorineural hearing loss with no vertigo [42]. Such a clinical presentation had been previously referred to as the cochlear form of the disease; however, the term has not been included in the current AAO-HNS guidelines [1, 3, 43], which state that at least two episodes of vertigo are required for the diagnosis of Ménière's disease.

The first study in which MRI scans were performed as part of the diagnostic protocol of endolymphatic hydrops had been carried out in patients without a history of typical vertigo and was published in 2009 by Teranishi et al. [44]. The authors demonstrated hydrops' presence within the cochlea and the vestibule in all eight patients, with fluctuating sensorineural hearing loss detected within the low-frequency range or across all audiometric frequencies.

Yoshida et al. [31] performed MRI scans in a group of patients with tinnitus as the main complaint. As in the study mentioned above by Teranishi et al. [44], the patients had no history of vertigo. The authors reported enlargement of the cochlear duct in 56% of symptomatic ears, with the grade of endolymphatic hydrops being significantly correlated with the presence of fluctuating tinnitus and the feeling of congestion within the ear.

The method has also found its use in patients with sudden idiopathic low-frequency sensorineural hearing loss. In a study by Shimono et al. [45], cochlear hydrops was detected in 92% of symptomatic ears following intratympanic administration of gadolinium contrast. It is worth noting that the enlargement of the endolymphatic space among people affected by the sudden low-frequency hearing loss was also observed within the vestibule, with vestibular hydrops developing in 88% of cases.

The above literature data show that the inner ear's MRI examinations facilitate diagnostics of patients with incomplete clinical presentation, including the predominance of audiological symptoms such as tinnitus or the feeling of congestion within the ear. The natural history of the Ménière disease should be considered, as these symptoms often precede the emergence of vertigo and evolution into a fully symptomatic form of the disease [46].

Cochlear and vestibular hydrops in patients with sudden low-frequency hearing loss are suggestive of the common pathogenesis of isolated sudden low-frequency hearing loss and fully symptomatic Ménière's disease MRI scans of the inner ear are likely to provide an opportunity for quicker diagnosis of endolymphatic hydrops in patients with early symptoms of the Ménière's disease.

A small percentage of patients with Ménière's disease experience transient improvement in hearing during vertigo episodes. Such a clinical presentation is referred to as the Lermoyez syndrome and is observed in about 0.2% of patients with Ménière's disease, although some researchers consider it a separate disease [47]. Zhou et al. [48] reported endolymphatic hydrops in all nine patients with Lermoyez syndrome in their study, which suggests that endolymphatic hydrops is involved in the pathogenesis of this clinical form of the disease. Importantly, compared with the results of patients with classic Ménière's disease, the grade of vestibular and cochlear hydrops was similar and significantly lower, respectively, in patients with Lermoyez syndrome [35]. It suggests that the variability of clinical presentations between individual subtypes of Ménière's disease manifests differences in endolymphatic hydrops' grades within individual inner ear structures.

THE ROLE OF MAGNETIC RESONANCE IN THE EVALUATION OF MÉNIÈRE'S DISEASE TREATMENT EFFICACY

The current guidelines for the management of Ménière's disease suggest an escalation approach. The treatment starts with dietary recommendations, lifestyle modification, and pharmacotherapy, while the next step consists of transtympanic treatment, i.e., steroids of aminoglycoside antibiotics being administered into the tympanic cavity. Upon no improvement, surgical methods are recommended in patients with persistent vertigo, including endolymphatic sac surgery and vestibular nerve section [1, 3].

Evaluation of the efficacy of the treatment of Ménière's disease is carried out mainly to reduce the incidence and severity of vertigo, which is considered the most burdensome disease symptom. However, the progressive nature of the disorder should be taken into account. It may lead to permanent damage to the organ of hearing and balance due to a continued increase in the endolymphatic volume. The use of MRI offers the possibility of assessing the hydrops' dynamics and thus control the pathological process within the inner ear.

Suga et al. analyzed the changes in the endolymphatic hydrops grades following conservative treatment [49]. They acquired MRI scans from a group of 12 patients with suspected Ménière's disease and then repeated the scans after 10 to 76 months. In the group of patients who reported subjective improvement, the hydrops grade was reduced in two out of three ears. At the same time, hydrops remission was observed in only one out of 17 ears, for which no resolution of symptoms was reported. In addition, Gurkov et al. [50] acquired MRI scans of six patients who had received beta-histidine at a dose of 2 × 24 mg for 3–7 months. The authors reported no changes in the grade of endolymphatic hydrops as a result of the treatment.

In a study by Fiorino et al. [51], the impact of transtympanic gentamycin on the degree of endolymphatic space enlargement was assessed in 8 patients. In follow-up MRI scans acquired 3–12 months after the baseline, no inner ear presentation changes were observed in four patients, whereas the other four patients presented with hydrops progression.

Literature reports are also available on MRI in the postoperative assessment of patients having undergone interventional procedures within the endolymphatic hydrops. Higashi-Shingai et al. [52] carried out an MRI study in 21 patients with Ménière's disease, who were subsequently qualified for endolymphatic sac drainage. A follow-up study performed two years after the procedure showed a significant reduction in vestibular hydrops' grade with no significant changes observed within the cochlea. Furthermore, the authors concluded that the regression of hydrops was not correlated with clinical improvement regarding the prevalence of vertigo, reducing the hearing threshold, or electrocochleographic examination results. Ito et al. [53] carried out a similar study in which they compared the hydrops' grade in 20 patients undergoing endolymphatic sac drainage procedures with intraoperative steroid administration. Two years after the procedure, the follow-up study revealed a link between the decrease in the hydrops' grade as assessed using the MRI and the degree of vertigo resolution.

The available literature presents only the preliminary results from studies conducted on small groups of patients with diverse disease durations and symptoms severities. In most of the above mentioned studies, the period between the baseline examination and the follow-up was as short as few months. Given the progressive, often multiannual natural history of Ménière's disease, long-term follow-up and scheduling of follow-up MRI scans in patients subjected to treatment may be of crucial importance.

SUMMARY

Despite many studies, the etiology of Ménière's disease remains unknown. The MRI examination of the inner ear offers the possibility of performing in vivo evaluation of the grade of endolymphatic hydrops, which is considered the disease's underlying cause. The analysis of correlations between the MRI results, clinical manifestations, and the audiologic and otoneurologic findings may be crucial to understanding the pathogenesis of the disease. In the treatment course, follow-up MRI scans enable the assessment of individual treatment modalities' efficacy in terms of the severity of lesions within the inner ear.

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Wodniak śródchłonki potwierdzony przy użyciu 3-teslowego skanera MR u pacjentów z obrazem klinicznym choroby Ménière'a

Endolymphatic Hydrops, Evaluated Using 3T MRI in Patients with Clinically Confirmed Meniere Disease

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STRESZCZENIE: Choroba Ménière'a charakteryzuje się występowaniem napadowych zawrotów głowy z towarzyszącym fluktuacyjnym niedosłuchem odbiorczym, szumami usznymi oraz uczuciem pełności w uchu. Pomimo wielu badań, etiologia choroby pozostaje nieustalona, a jej diagnoza opiera się w głównej mierze na obrazie klinicznym, który charakteryzuje się dużą zmiennością osobniczą i fluktuacyjnym przebiegiem. Możliwość obrazowania ucha wewnętrznego metodą rezonansu magnetycznego po raz pierwszy została opisana w 2007 roku i okazała się znacznym przełomem w diagnostyce wodniaka endolimfatycznego. Prezentujemy opis dwóch przypadków pacjentów z obrazem klinicznym sugerującym chorobę Ménière'a, u których został wykonany pakiet badań audiologicznych, otoneurologicznych, a także rezonans magnetyczny ucha wewnętrznego. W badaniu obrazowym, struktury przedsionka oraz ślimak zostały ocenione po czterech godzinach od podania podwójnej dawki kontrastu gadolinowego dożylnie za pomocą skali zaproponowanej przez Baratha. U opisywanych chorych potwierdzono obecność wodniaka śródchłonki po stronie objawów klinicznych w badaniu MR. Z uwagi na znaczne zaawansowanie kliniczne choroby, opisywani pacjenci zostali zakwalifikowani do chirurgicznego leczenia poprzez przecięcie nerwu przedsionkowego z dostępu przez dół środkowy czaszki.

SŁOWA KLUCZOWE: choroba Ménière'a, rezonans magnetyczny ucha wewnętrznego, wodniak endolimfatyczny

ABSTRACT: Ménière's disease (MD) is characterised by intermittent episodes of vertigo with fluctuating sensorineural hearing loss, tinnitus and aural fullness. Despite numerous studies, the etiology of this disorder remains poorly understood and thus diagnostic criteria are mainly clinical. Development and progress in magnetic resonance imaging (MRI) techniques, in 2007, has enabled visualisation of endolymphatic hydrops, which was the milestone achievement. We present two cases of patients with clinically confirmed MD with a set of audiological, otoneurological examinations and MRI performed. Structures of the inner ear were visualized using contrast-enhanced MR imaging after a 4-hour delayed intravenous gadolinium administration. The cochlea and vestibule were evaluated separately and classified using Barath grading scale. Endolymphatic hydrops in the clinically affected ears were confirmed using MRI. Due to disabling and intractable MD, a decision about vestibular neurectomy was made.

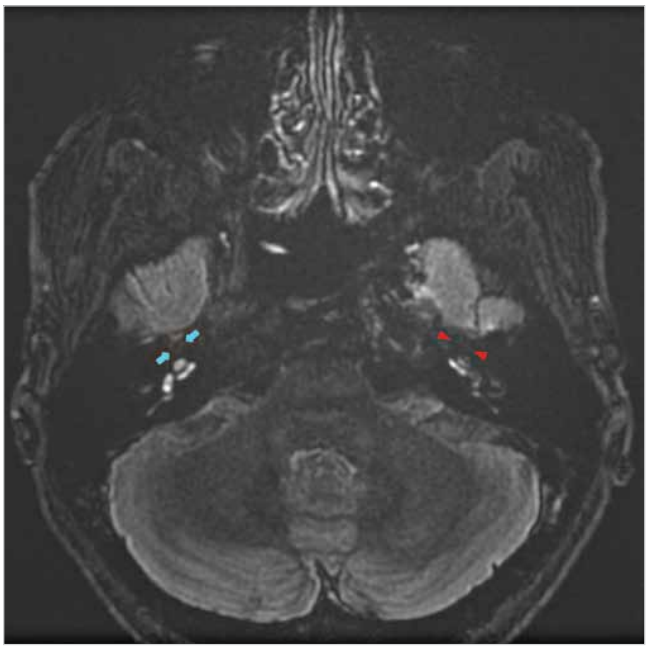
KEYWORDS: endolymphatic hydrops, inner ear magnetic resonanse, Ménière's disease

WYKAZ SRÓTÓW

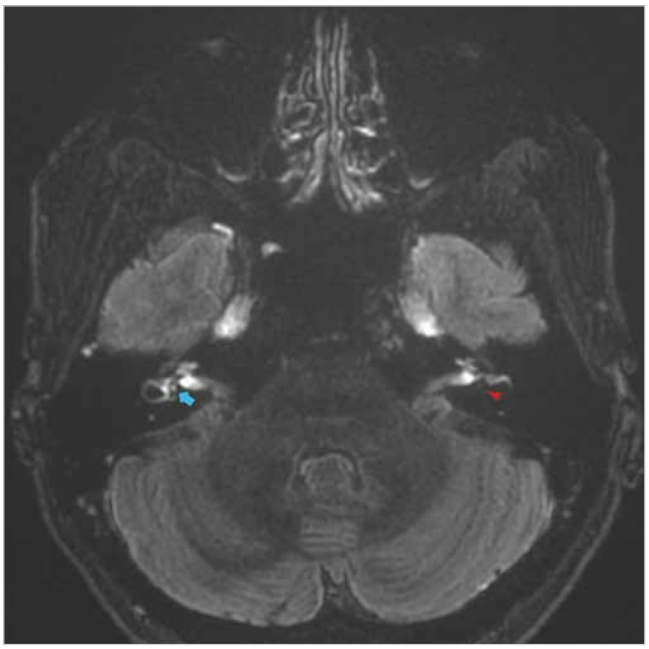
AAO-HNS – Komitet ds. Słuchu i Równowagi Amerykańskiej Akademii Otolaryngologii i Chirurgii Głowy i Szyi
MR lub MRI – Rezonans Magnetyczny

WPROWADZENIE

W 1861 r. Prosper Ménière, w swojej pracy opublikowanej na łamach „Gazette Médicale de Paris", jako pierwszy powiązał występowanie zawrotów głowy z patologią ucha wewnętrznego [1]. Stanął tym samym w opozycji do ówczesnych badaczy, którzy podobne dolegliwości wiązali wyłącznie z ośrodkowym układem nerwowym. Opisana przez niego triada objawów: napadowe wirowe zawroty głowy, niskotonowy niedosłuch oraz szumy uszne lub uczucie pełności w uchu, zostały określone chorobą Ménière'a. Morfologiczne podłoże tych objawów potwierdzili prawie 80 lat później Cairns, Hallpike oraz Yamakawa, którzy, analizując preparaty kości skroniowych pacjentów z obrazem klinicznym odpowiadającym chorobie Ménière'a, stwierdzili obecność rozdętych przestrzeni endolimfatycznych, nazwanych następnie *wodniakiem śródchłonki* [2, 3]. Z powodu pośmiertnego



Ryc. 1. 65-letnia kobieta z podejrzeniem choroby Ménière'a po stronie lewej. Przekrój osiowy na poziomie ślimaków, w sekwencji 3D FLAIR, 4 godziny po dożylnym podaniu podwójnej dawki środka cieniującego. Po stronie lewej widoczny poszerzony, niewzmacniający się przewód ślimakowy w znacznym stopniu zwężający schody przedsionka. Obraz odpowiada stopniowi II wodniaka ślimaka wg klasyfikacji Baratha (czerwone strzałki). Po stronie prawej obraz prawidłowo wzmacniających się struktur perylimfatycznych ślimaka i brak poszerzenia struktur endolimfatycznych (niebieskie strzałki).



Ryc. 2. 65-letnia kobieta z podejrzeniem choroby Ménière'a po stronie lewej. Przekrój osiowy na poziomie przedsionków, w sekwencji 3D FLAIR, 4 godziny po dożylnym podaniu podwójnej dawki środka cieniującego. Po stronie lewej widoczne poszerzone woreczek i łagiewka, nie jest widoczne brzeżne wzmocnienie przedsionka. Obraz odpowiada stopniowi II wodniaka przedsionka wg klasyfikacji Baratha (czerwona strzałka). Po stronie prawej obraz prawidłowego wzmocnienia przedsionka oraz nie wzmacniających się woreczka i łagiewki (niebieska strzałka).

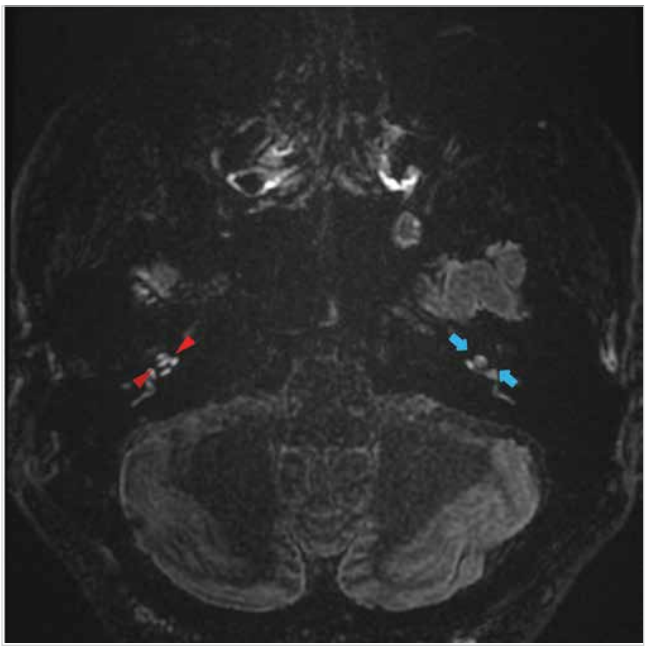
charakteru badania histopatologicznego, które jako jedyne pozwalało na potwierdzenie wodniaka endolimfatycznego, rozpoznanie choroby Ménière'a pozostało diagnozą kliniczną, stawianą na podstawie typowego zespołu objawów i udokumentowanego niedosłuchu [4]. Fluktuacyjny, zmienny osobniczo i nieprzewidywalny przebieg choroby utrudnia proces diagnostyczny i często opóźnia postawienie rozpoznania nawet o kilka lat. Znaczącym przełomem okazała się możliwość obrazowania wodniaka endolimfatycznego *in-vivo* w MR, opisana przez Nakashimę i wsp. w 2007 r. [5]. Podali oni kontrast gadolinowy do jamy bębenkowej i zaobserwowali, że w sekwencji FLAIR (*Fluid-attenuated inversion recovery*) migruje on do struktur perylimfatycznych, a struktury endolimfatyczne pozostają niezakontrastowane. W 2014 r. Naganawa i wsp. ustalili, że ten sam efekt można uzyskać, podając podwójną dawkę kontrastu dożylnie [6].

Aktualnie stosowane protokoły opierają się na metodzie zaproponowanej przez Naganawę, tj. oceny dokonuje się w sekwencji FLAIR 3D po czterech godzinach od podania podwójnej dawki kontrastu gadolinowego drogą dożylną. Chorobę Ménière'a podejrzewa się u pacjentów z poszerzonymi strukturami endolimfatycznymi, które nie ulegają wzmocnieniu kontrastowemu i w tej sekwencji widoczne są jako ubytki zakontrastowania na tle wzmacniających się struktur perylimfatycznych. Stopień nasilenia wodniaka struktur endolimfatycznych ocenia się z użyciem klasyfikacji zaproponowanej przez Baratha i wsp. [7]. Stopień nasilenia wodniaka struktur endolimfatycznych ślimaka oraz przedsionka ocenia się w niej osobno. Dla ślimaka stopień 0 oznacza brak poszerzenia przewodu ślimakowego, stopień I – częściowe poszerzenie przewodu ślimakowego, stopień I częściowe poszerzenie przewodu ślimakowego, z widocznym zwężeniem schodów przedsionka, natomiast stopień II – całkowite poszerzenie przewodu ślimakowego tak, że schody przedsionka stają się niewidoczne. Analogicznie dla przedsionka: stopień 0 to brak poszerzenia łagiewki i woreczka, stopień I – powiększenie się woreczka i łagiewki tak, że nie jest widoczna granica między nimi, a widoczne jest brzeżne wzmocnienie przedsionka, zaś stopień II oznacza tak znaczne poszerzenie łagiewka i woreczka, że nie jest widoczny przedsionek.

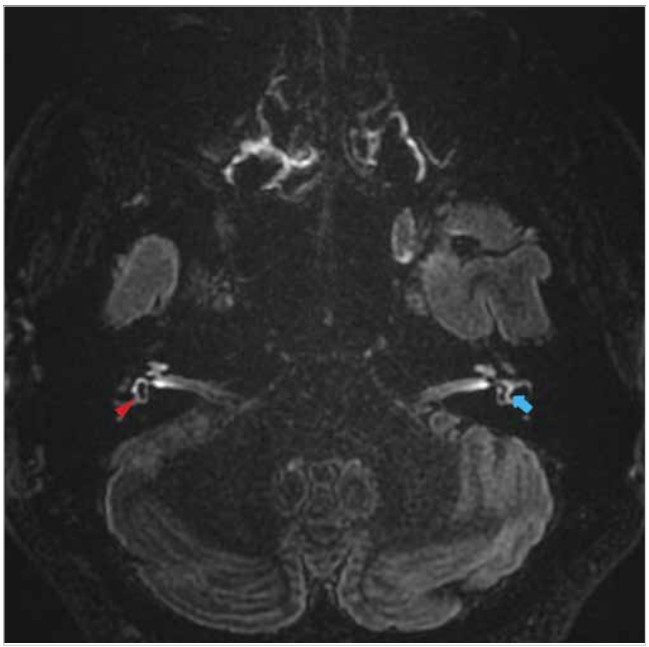
OPIS PRZYPADKÓW

Przedstawiono opis dwóch pacjentów z podejrzeniem choroby Ménière'a, którzy zostali przyjęci do Kliniki Otorynolaryngologii, Chirurgii Głowy i Szyi Warszawskiego Uniwersytetu Medycznego w celu przeprowadzenia diagnostyki audiologicznej i otoneurologicznej. Proces diagnostyczny obejmował: dokładne badanie podmiotowe i przedmiotowe, audiometrię tonalną, słowną i impedancyjną, badanie emisji otoakustycznych, potencjałów wywołanych pnia mózgu, elektrokochleografię, widonystygmografię oraz badanie obrazowe ucha wewnętrznego przy użyciu 3-teslowego skanera MR (GE, SIGNA Architect, Milwaukee, USA). Struktury przedsionka oraz ślimaka oceniono po czterech godzinach od dożylnego podania podwójnej dawki kontrastu gadolinowego (gadobutrol), na co uzyskano zgodę komisji bioetycznej oraz pacjentów.

W ocenie radiologicznej struktur ucha wewnętrznego została użyta klasyfikacja zaproponowana przez Baratha.



Ryc. 3. 59-letni mężczyzna z podejrzeniem choroby Ménière'a po stronie prawej. Przekrój osiowy na poziomie ślimaków, w sekwencji 3D FLAIR, 4 godziny po dożylnym podaniu podwójnej dawki środka cieniującego. Po stronie prawej widoczny poszerzony, niewzmacniający się przewód ślimakowy w umiarkowanym stopniu zwężający schody przedsionka. Obraz odpowiada stopniowi I/II wodniaka ślimaka wg klasyfikacji Baratha (czerwone strzałki). Po stronie lewej obraz prawidłowo wzmacniających się struktur perylimfatycznych ślimaka i brak poszerzenia struktur endolimfatycznych (niebieskie strzałki).



Ryc. 4. 59-letni mężczyzna z podejrzeniem choroby Ménière'a po stronie prawej. Przekrój osiowy na poziomie przedsionków, w sekwencji 3D FLAIR, 4 godziny po dożylnym podaniu podwójnej dawki środka cieniującego. Po stronie prawej widoczne nieznacznie poszerzenie woreczka i łagiewki, widoczne jest brzeżne wzmocnienie przedsionka. Obraz odpowiada stopniowi 0/I wodniaka przedsionka wg klasyfikacji Baratha (czerwona strzałka). Po stronie lewej obraz prawidłowego wzmocnienia przedsionka oraz nie wzmacniających się woreczka i łagiewki (niebieska strzałka).

Przypadek 1.

65-letnia pacjentka, u której pierwszy typowy napad zawrotów głowy, z towarzyszącym uczuciem pełności w uchu i pogorszeniem słuchu po stronie lewej, wystąpił przed 8 laty. Chora podawała niskotonowe szumy uszne, których średnie nasilenie w okresie ostatnich 6 miesięcy wynosiło 4,75 w skali od 0 do 6 zaproponowanej przez Arenberga, oraz fluktuacyjne, postępujące wraz z czasem trwania choroby, pogorszenie słuchu po stronie lewej. W wykonanej audiometrii tonalnej stwierdzono znacznego stopnia pantonalny niedosłuch odbiorczy ucha lewego. Analiza wyników badania potencjałów wywołanych pnia mózgu wskazywała na uszkodzenie odbiorcze typu ślimakowego w po stronie lewej. W badaniu MRI ucha wewnętrznego zaobserwowano poszerzony przewód ślimaka, powodujący całkowitą obliterację wodociągu przedsionka (stopień II wodniaka ślimakowego wg Baratha) oraz znacznego stopnia powiększenia łagiewki i woreczka, z niewidocznym brzeżnym wzmocnieniem przedsionka (stopień II wodniaka przedsionka) (Ryc. 1.–2.). Po stronie prawej obraz ucha wewnętrznego w badaniu obrazowym był prawidłowy.

Omawiana pacjentka przyjmowała przewlekle betahistynę w dawce 24 mg 2 razy dziennie; podjęta była także próba leczenia diuretykami oraz sterydoterapii drogą transtympanalną. W subiektywnej ocenie chora określiła stopień nasilenia objawów oraz wpływ dolegliwości na codzienne funkcjonowanie na stopień IV w VI-stopniowej skali zaproponowanej przez AAO-HNS. Z uwagi na zaawansowanie kliniczne choroby oraz nieskuteczność wcześniejszego leczenia, na podstawie analizy wyników przeprowadzonych badań audiologicznych, otoneurologicznych oraz obrazowych, pacjentka została zakwalifikowana do neurektomii przedsionkowej z dostępu przez środkowy dół czaszki. Okres okołooperacyjny przebiegł bez powikłań. Planowane są kontrolne badania audiologiczne, otoneurologiczne, a także badanie MRI ucha wewnętrznego chorej po 6 miesiącach.

Przypadek 2.

59-letni mężczyzna z rocznym wywiadem sugerującym chorobę Ménière'a. Pierwszym objawem był typowy napad zawrotów głowy z towarzyszącym uczuciem pełności w uchu prawym, szumem usznym oraz subiektywnym pogorszeniem słuchu po tej stronie. W ciągu pierwszych 6 miesięcy od rozpoczęcia choroby pacjent doświadczał średnio 6,5 typowych napadów miesięcznie. Następnie doszło do trwającej ponad 4 miesiące samoistnej remisji choroby, przerwanej dwoma napadami w ostatnim miesiącu. W skali funkcjonalnej subiektywne średnie nasilenie pełności w uchu w ciągu 12 miesięcy trwania choroby wynosiło 4 w skali Arenbegra. Szumy uszne w tym okresie były ocenione średnio na 3,45 w podobnej skali. W badaniu audiologicznym, wykonanym w okresie bezobjawowym, stwierdzono niedosłuch odbiorczy, obejmujący tony średnie oraz wysokie. Zapisy elektrokochleografii transtympanalnej wskazywały na ewidentne cechy wodniaka błędnika po stronie prawej.

W badaniu MR zaobserwowano częściowe poszerzenie przewodu ślimaka (stopień I/II) oraz brak niewielkie poszerzenie woreczk-

ka i łagiewki na tle wzmacniającego się przedsionka (Ryc. 3.–4.). Z uwagi agresywny, szybko postępujący przebieg kliniczny choroby oraz znaczne upośledzenie codziennego funkcjonowania pacjenta (stopień V w VI-stopniowej skali), został on zakwalifikowany do leczenia chirurgicznego i obecnie oczekuje na operację przecięcia nerwu przedsionkowego.

OMÓWIENIE

Pomimo wielu przeprowadzonych badań, etiologia choroby Ménière'a pozostaje nieustalona, a rozpoznanie opiera się w głównej mierze na obrazie klinicznym. Wiadomo jednak, że objawy spowodowane są zaburzeniami równowagi hydrostatycznej i osmotycznej pomiędzy śródchłonką a przychłonką, w wyniku których powstaje wodniak śródchłonki [8, 9]. Możliwość obrazowania poszerzonych przestrzeni endolimfatycznych ucha wewnętrznego przy pomocy 3-teslowego rezonansu magnetycznego stanowi niezwykle istotną, mało inwazyjną metodę pozwalającą na potwierdzenie obecności wodniaka. Liczne badania potwierdziły korelację pomiędzy obrazem klinicznym a zaawansowaniem choroby w badaniu obrazowym [10, 11]. Opisywano przypadki pacjentów, u których cechy poszerzenia przestrzeni endolimfatycznych w klinicznie zdrowym uchu zostały wykryte metodą rezonansu magnetycznego, co sugeruje możliwość zobrazowania wodniaka przed wystąpieniem objawów klinicznych [12]. Szczególnie istotną wartość diagnostyczną ma MRI ucha wewnętrznego w grupie chorych, którzy nie prezentują pełnego obrazu klinicznego choroby Ménière'a. Wskazują na to prace potwierdzające obecność wodniaka endolimfatycznego w badaniu obrazowym u pacjentów z nietypowym przebiegiem choroby [13].

Agresywny przebieg choroby z częstymi, uporczywymi atakami zawrotów głowy, przy braku poprawy pomimo leczenia zachowawczego i podawania leków do jamy bębenkowej, jest wskazaniem do leczenia chirurgicznego. W trakcie kwalifikacji chorego do skutecznej, jednak inwazyjnej procedury przecięcia nerwu przedsionkowego, pomocne może okazać się potwierdzenie obecności wodniaka śródchłonki jako przyczyny objawów. Obrazowania ucha wewnętrznego przy użyciu MR może być także elementem oceny skuteczności leczenia pacjentów z objawami choroby Ménière'a [14].

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Correlation between magnetic resonance imaging classification of endolymphatic hydrops and clinical manifestations and audiovestibular test results in patients with definite Ménière's disease ☆

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ABSTRACT

Objectives: The purpose was to evaluate magnetic resonance imaging (MRI) classification of endolymphatic hydrops with clinical features, audiological and vestibular tests in patients with definite unilateral Ménière's disease (MD).

Methods: Thirty-eight patients were enrolled in this study. The severity of the main clinical symptoms, audiovestibular tests, and MRI, performed 4 hours after intravenous injection of gadobutrol to visualize inner ear compartments, were evaluated. Endolymphatic space dilatation was assessed using Barath and Bernaerts grading systems, and the correlation between the grade of the hydrops and clinical features was evaluated.

Results: Using the Barath system, cochlear hydrops was visualized in 81.6% of affected ears, while vestibular was 63.2%. Sensitivity increased to 94.7% using Bernaerts' modification. Vestibular hydrops involving the utricle was present only among patients with cochlear and saccular endolymphatic space dilatation. There was a significant relationship between the hearing level and the vestibular hydrops degree in the Bernaerts scale. The grade of the hydrops correlated neither with the duration of MD nor with the severity of main clinical symptoms. Our study proved MRI to be a sensitive diagnostic tool in MD. The endolymphatic hydrops' grade correlates with the hearing level, which confirms endolymphatic space dilatation's role in hearing loss.

Conclusions: In our study, two similar MRI grading systems were used; however, several differences were found compared to one another. The Bernaerts scale was more sensitive than the Barath scale, and several relationships between the radiological and clinical data were found. Therefore, several MRI evaluating scales and correlating them with the clinical features are needed. The increased perilymphatic enhancement of the cochlea and an extra low-grade vestibu-

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lar hydrops distinguished in the Bernaerts scale may increase MD diagnosis sensitivity. Magnetic resonance findings in MD support the clinical diagnosis and may help to understand MD pathophysiology better. This study adds to the knowledge and diagnostics in MD for healthcare to improve patients' treatment.

1. Introduction

Ménière's disease (MD) is a chronic inner ear disorder characterized by vertigo episodes with fluctuating low-frequency hearing loss, tinnitus, and aural fullness. Its etiology remains unknown, but the endolymphatic hydrops (EH) is considered underlying pathology since Hallpike and Cairns, and Yamakawa [1,2] reported the presence of dilated endolymphatic spaces in the temporal bones of patients with symptoms of MD. From that time, confirmation of the EH was possible, but the certain MD diagnosis was made only post-mortem.

According to the guidelines established in 1995 and revised in 2020 by the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) and the Bárány Society criteria formulated in 2015, diagnosis of MD remains based on clinical manifestation [3–5]. However, due to the recent development of magnetic resonance technology, visualization of enlarged endolymphatic space allowed to objectify the underlying morphological hallmark of MD. In 2007, Nakashima et al. [6] reported in-vivo EH imaging's first research using 3-dimensional magnetic resonance imaging (3D-MRI). In MRI sequences, the inner ear's compartments are distinguished due to the signal differences caused by the contrast agent's heterogeneous penetration – gadolinium is accumulated in the perilymph and does not reach the endolymph. Thus, EH is visualized as a partial loss of contrast enhancement in the areas usually occupied by perilymph. Over the last decade, several studies concerning MR imaging of the inner ear were completed using rearranged methods and protocols. We can distinguish two different gadolinium-based contrast material (GBCM) delivery methods: intratympanic and intravenous injection. The intravenous route of contrast administration is more widely used because of its less invasive character and the possibility of simultaneously evaluating both ears. Besides, it requires only 4 hours before image acquisition compared to a 24 h waiting time using intratympanic injections.

Several EHI evaluation methods already exist and can be divided into qualitative, semi-quantitative, and volumetric techniques. The first documented criteria proposed ten years ago by Nakashima et al. [7] consist of a semi-quantitative grading score based on a single-slice-analysis. The vestibule and the cochlea are assessed separately in one axial slice of MRI; in the vestibule, the ratio of the endolymphatic space over the total fluid area in the inner ear (sum of the endolymphatic and perilymphatic spaces) is evaluated, whereas in the cochlea the displacement of the Reissner's membrane, as a mark of scala media enlargement, is taken into account. According to these criteria, vestibular and cochlear endolymphatic hydrops can be assessed as none, moderate and severe. Although this single-slice-analysis allows a fast evaluation of EH, the proportions of the endolymphatic and perilymphatic spaces can vary between patients depending on the head position during MR examination or anatomical features in the temporal bones. Barath et al. [8] proposed a grading system based on a visual comparison of contrast-enhanced perilymphatic and non-enhanced endolymphatic spaces in the cochlea and vestibule separately. The Barath grading system was recently revised and modified by Bernaerts et al. [9]. They added a lower grade I as a least severe stage based on saccular enlargement to the vestibular hydrops assessment.

Several studies have proven that MRI is a reliable diagnostic method of EH detection, with a sensitivity up to 90%, which makes it comparable to histopathological examination [8].

In healthy individuals in the cochlea, the endolymphatic scala media (cochlear duct) is barely visible between enhancing filled with perilymph scala tympani and scala vestibuli [8]. In the normal vestibule, the endolymphatic structures saccule and utricle do not exceed 1/3 of the whole vestibular space [7], they can be easily differentiated [8], and the saccule is smaller than the utricle [10,11]. Furthermore, in healthy individuals, the enhancement of the inner ear structures is symmetric, comparing both sides with each other. Ito et al. [12] were the first who compared a group of patients with MD with healthy volunteers and reported that EH was present in 6.3% of asymptomatic ears of MD patients and 10% of healthy volunteers' ears. In contrast, in the MD group, EH was observed in 81% of patients. Seo et al. [13] reported that EH wasn't present only in 0.04% of patients with definite MD, and Barath et al. [8] described that EH was present in 90% of MD patients' affected ears and 22% of unaffected ears. Recently van Steekelenburg et al. [14] found that EH was present in 92% of patients with definite MD and only in 4.7% of contralateral healthy ears. The mentioned studies described MD's inner ear space as significantly larger than healthy controls or unaffected contralateral ear. This feature implies the usefulness of MR enhanced with contrast media for the recognition of an ear affected by Meniere's disease.

Correlation between the MRI, clinical manifestations of MD, and various otological tests were reported in several studies with variable opposed conclusions formed [15–18]. As the next grading systems for EH are established, there is a need to correlate them with the clinical features. Moreover, the relationship between the self-estimated current severity of symptoms and EH remains unclear.

Our study aimed to analyze whether the cochlear and vestibular endolymphatic space's dilatation observed in MRI

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is correlated with the severity of MD symptoms or audiovestibular test results. Our purpose was to evaluate the Barath grading system and its modification proposed by Bernaerts regarding clinical features, audiological and vestibular tests in patients with definite MD.

2. Material and methods

2.1. Ethical consideration

The Institutional Ethics Committee at the Medical University of Warsaw approved the study protocol (KB/110/2019). The project conforms to The Code of Ethics of the World Medical Association (Declaration of Helsinki). All patients gave their written informed consent for participation in the study.

2.2. Patients description

Thirty-eight patients clinically diagnosed with unilateral definite Meniere's disease based on the AAO-HNS and the Barany Society guidelines were enrolled in this study.

2.3. Study protocol

The main clinical symptoms were evaluated in the past six months. An average frequency of vertigo spells per month was calculated, the mean severity of tinnitus, aural fullness, and balance problems was rated with a 0-6 scale proposed by Arenberg and Stahle [19]. The patient's functional level was estimated using a 1-6 AAO-HNS grading scale [3].

The examination was performed during a vertigo-free interval. The exclusions criteria were as follows: bilateral MD, past medical history of chronic otitis media, otosclerosis, ear surgery in the past, or MR-related contradictions.

2.4. Audiovestibular tests

Patients underwent standard pure-tone audiometry, speech audiometry, impedance audiometry, and auditory brainstem response (ABR) test on the first day of hospitalization.

The pure tone average (PTA) hearing levels were calculated as the mean values among air-conduction hearing threshold levels at 500, 1000, 2000, and 4000 Hz. Still, low frequency of 250 Hz was evaluated as well.

ABR test was performed using a Smart Box device with Smart EP software (Intelligent Hearing Systems, FL, Miami, USA). Click stimuli at 90 dBnHL intensity and repetition rate of 27.7/s were presented monaurally using ER3-A insert earphones (Etymotic Research, Elk Grove Village, IL). Ipsilateral responses were collected and saved in 3 blocks of 1024 sweeps. The results were divided into four groups: normal response, cochlear hearing loss pattern, retrocochlear hearing loss pattern, and complete absence of response.

Videonystagmography (VNG) examination using the Micromedical system (Micromedical Technologies Inc., Chatham, USA) was performed. Caloric responses after irrigation of 30 and 44 °C water were assessed. Results on the affected side were evaluated compared to the contralateral ear and divided into four groups: symmetrical caloric responses, unilateral caloric vestibular weakness, central vestibular dysfunction, and vestibular paresis on the affected side.

Transtympanic electrocochleography (TT-ECochG) was performed using the Smart Box device with Smart EP software (Intelligent Hearing Systems, FL, Miami, USA). ECochG was planned as the last test to avoid impact on other electrophysiological tests because the recording needle electrode requires to be entered through a puncture in the tympanic membrane. The examination was conducted monaurally with click stimuli of 90 dBnHL presented at a rate of 49.9/s. Ipsilateral responses were collected and saved in 3 blocks of 256 sweeps. The average result was then assigned, and the summating potential to action potential (SP/AP) ratio was calculated. The SP/AP ratio >0.33 was considered abnormal. Although TT-ECochG is known to have diagnostic value in estimating endolymphatic hydrops, no particular SP/AP ratio value has been established to indicate Meniere's disease. Several cut-off values standing from 0.29 to 0.50 were proposed. In our department, for the device used, we recognize a value of 0.33 (verified earlier in our department in healthy controls), which is in agreement with other studies performed by Seo et al. [13] and Fukuoka et al. [20] that compared TT-ECoChG results and hydrops severity in MRI. However, in our study, we also decided to correlate hydrops degree with the SP/AP as a numerical variable to get more accurate results and avoid the misassignment of patients with SP/AP 0.3–0.49 if it was analyzed as an ordinal variable.

2.5. Magnetic resonance imaging analysis

MRI scans of all participants were performed using a 3 Tesla MR scanner (Signa Architect, GE Healthcare, Milwaukee, USA) with a 16-channel flex coil (GEM Flex Large coil, Neocoil, Pewaukee, USA).

The standard protocol for Meniere disease included two 3D-FLAIR sequences; the first performed without contrast media and the second 4 hours after intravenous contrast administration. A double dose of gadobutrol (Gadovist; Bayer Schering Pharma AG, Berlin, Germany; 1.0 mmol/mL) at a dose of 0.2ml/kg was used to achieve a maximum perilymphatic enhancement, as was described previously in the literature [8,16]. The 3D-FLAIR sequence was performed with the following parameters: TR 7602 ms, TE 170ms, TI 1897; 180° flip angle (constant), FOV 18, matrix 232 × 232 mm, NEX 2.0. Our study used a conventional turbo spin-echo 3-dimensional fluid-attenuated inversion recovery (3D-FLAIR) sequence with a constant 180° flip angle. When using this sequence, after a single dose of gadolinium, the enhancement of perilymph is so faint that it is impossible to distinguish endolymphatic structures from perilymphatic space [21–23], and after a double dose of gadolinium, the perilymph shows higher levels of signal. A single dose of contrast media may be used with Heavily T2-Weighted 3D-FLAIR and 3D-IR with real reconstruction sequences, which are not widely available. Furthermore, the 3D-IR sequence is significantly

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Table 1. Barath and Bernaerts scales for cochlear and vestibular endolymphatic hydrops evaluation with magnetic resonance imaging (MRI).

Cochlear endolymphatic hydrops evaluation		
Barath scale		**MRI features description**
normal		the non-enhancing cochlear duct barely visible between enhancing scala vestibuli and tympani
grade I		partial obstruction of the scala vestibuli by a mildly dilated cochlear duct
grade II		cochlear duct so distended that fully obliterate scala vestibuli
Vestibular endolymphatic hydrops evaluation		
Barath scale	**Bernaerts scale**	**MRI features description**
normal	**normal**	non-enhancing saccule and utricle easily visible in the enhancing vestibule and saccule smaller than utricle
	grade I	saccule equal or larger than the utricle but still separated
grade I	**grade II**	dilatation of saccule and/or utricle present with circular enhancing perilymphatic space
grade II	**grade III**	dilation of saccule and utricle caused no enhancing perilymphatic space visible

longer and more sensitive to motion artifacts than the 3D-FLAIR sequence [24].

The obtained MR images were analyzed by a head and neck radiologist (one of the authors). Endolymphatic hydrops was categorized using Barath [8] and Bernaerts [9] grading systems presented in Table 1.

Barath et al. assessed endolymphatic hydrops separately for cochlea and vestibule. The Barath criteria defined a three-stage grading system of endolymphatic hydrops (none, grade I, and grade II).

Bernaerts et al. modified Barath's vestibular hydrops criteria by adding extra low-grade vestibular hydrops when the saccule is enlarged but still separated from the utricle, so the Bernaerts scale has four stages for the vestibule. What is more, the author included a semi-quantitative evaluation of the perilymphatic enhancement of the affected ear compared to the opposite side.

Our study did not include healthy individuals as a control group. In MD patients, contralateral ears should be distinguished from the healthy control ears. Endolymphatic hydrops can develop within years in the contralateral ear in patients with unilateral MD before clinical symptoms from that ear start. In our study, to evaluate endolymphatic hydrops, we chose the qualitative scale where each ear is assessed separately; therefore, there was no need to compare them to healthy controls. Furthermore, in our study, we did not refer to our patients' contralateral ears as healthy ears. According to the Bernaerts criteria [9], the affected ears and the contralateral ears in each particular patient were evaluated when assessing the perilymphatic enhancement of the cochlea as it is included in the criteria. Still, it does not mean that the contralateral ears were considered completely healthy. The contralateral ears in our patients were asymptomatic and presented normal test results. However, as mentioned before, it should be kept in mind that in MD patients, the contralateral ear might get affected after many years.

2.6. Statistical analysis

Statistical analysis was carried out in the STATISTICA program (StatSoft, Inc. 2017 analysis software system, version 13.3). The data were tested for normality, parametric and non-parametric criteria. Detailed statistical analysis was performed with the following tests: Spearman's correlation, the Mann-Whitney U test, Wilcoxon signed-rank test. The level of statistical significance was set at $p = 0.05$.

3. Results

Patients' characteristics are presented in Table 2. Thirty-eight patients clinically diagnosed with unilateral definite Meniere's disease (13 in the right ear, 25 in the left) were enrolled in this study. Among them, 19 were males and 19 females, mean age 54.39, MD duration from 0.5 to 21 years (mean 7.73 years). The average frequency of vertigo attacks in the last six months was 3.25 ± 3.09 per month. Seven patients (18.42%) suffered from Tumarkin drop attacks. Subjective severity of tinnitus, aural fullness, and balance problems in vertigo-free intervals varied among patients from minimum to maximum on the Arenberg scale. The average functional level was 4.21 ± 0.96 on the 6-point AAO-HNS scale.

3.1. Audiovestibular tests

The mean PTA level was 51.58 dBHL (±18.07 dB) in the affected ear in audiometric tests. The average hearing threshold for 250 Hz frequency was 54.05 dBHL (±18.17 dB). Out of 38 patients, only 2 had a normal hearing with PTA levels ≤20 dBHL. Spearman's correlation test revealed that PTA level in the affected ear was correlated with age ($p = 0.0162$), with the strongest correlation between age and hearing level at 4 kHz ($p = 0.0008$).

The analyzes revealed that hearing levels differed between affected and asymptomatic ears at all frequencies examined (for all results of Wilcoxon signed-rank test $p = 0.0000$).

The ABR results pointed to cochlear hearing loss in 39.47% of the affected ears. Other patterns of the ABR results were less common: 31.58% of analyzed ears presented normal responses, 21.05% retrocochlear hearing loss, and 5.26% no response.

Abnormal TT-EChoG responses were observed in 73.68% of the affected ears, including 27 patients with SP/AP ratio > 0.33 and one patient with no response due to severe hearing loss. The average SP/AP ratio was 0.62 (±0.49) in the symptomatic ears. In 15.79% of the clinically affected ears, SP amplitude was higher than the AP amplitude (SP/AP >1) (Fig. 1).

Unilateral vestibular weakness was observed among the affected ears in 63.16%, while complete vestibular paresis oc-

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Table 2. Clinical characteristics of the analyzed patients' population with Meniere's disease.

	mean	median	min	max	SD
age (years)	54.39	58.00	30.00	77.00	11.18
duration of Ménière's disease (years)	7.73	6.50	0.50	21.00	5.69
duration of vertigo (years)	6.08	5.00	0.25	21.00	5.16
avg number of vertigo spells* (number/month)	3.25	2.33	0.00	11.66	3.09
average tinnitus* (0-6 Arenberg scale)	4.04	4.17	0.00	6.00	1.43
average imbalance* (0-6 Arenberg scale)	3.01	3.25	0.00	6.00	1.53
average aural fullness* (0-6 Arenberg scale)	2.70	2.33	0.00	6.00	1.64
functional level (AAO HNS 1-6 scale)	4.21	4.00	2.00	6.00	0.96

min - minimum, max - maximum, SD - standard deviation
* during last six months

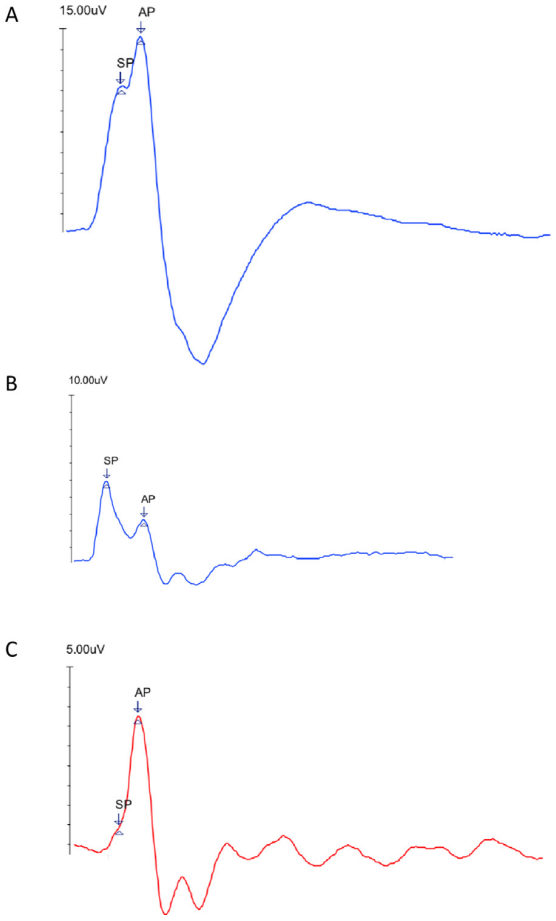

Fig. 1. Transtympanic electrocochleography (TT-ECochG) results of patients with defined Ménière's disease (MD). (A) The summating potential to action potential (SP/AP) ratio of 0.72 indicates endolymphatic hydrops in a 62-year-old woman with MD lasting seven years. The pure tone average (PTA) hearing level was 57.5 dB; (B) The summation potential amplitude elevated above the action potential amplitude (SP/AP ratio 2.08) in a 46-year-old woman with an MD duration of 9 months. A PTA level of the affected ear was 45 dB in this case; (C) Normal TT-ECochG result with SP/AP=0.24 in a 65-year-old woman suffering from MD for nine years with a PTA level of 66.25 dB in the affected ear. In all of these 3 cases, in MRI scans, endolymphatic hydrops was found on the affected side- grade I in the cochlea and the vestibule according to the Barath evaluation system.

curred in 13.16%. 18.42% of the symptomatic ears presented normal caloric responses, whereas central vestibular dysfunction in the VNG test was found in 5.26 %.

3.2. MRI data

Radiological data of images analyzed with Barath and Bernaerts scales are presented in Table 3, Fig. 2. Analyzing MRI scans with the Barath grading system, cochlear EH was visualized in 81.6% of affected ears, while vestibular EH in 63.2%. Sensitivity increased to 92,1% using Bernaerts' modification as saccule equal to or larger than utricle, as the only sign of the EH, was visualized in 4 patients. When analyzing vestibular endolymphatic space, a significant difference in EH detection was found comparing Barath and Bernaerts scales ($p = 0.0033$) as in 78.57% of patients with a normal vestibule in the Barath scale the EH was found using Bernaerts scale. Considering increased perilymphatic enhancement on the affected side as an additional but sufficient to recognize MD radiological sign, the sensitivity reached 94.74%.

In three patients, MRI scans did not show endolymphatic hydrops based on Bernaets classification. Two of them had normal hearing levels, though the SP/AP ratio in these cases was elevated. Only one patient had neither dilated endolymphatic space in MRI nor an abnormal SP/AP ratio. However, the perilymphatic enhancement of the cochlea and the vestibule on the affected side was significantly increased compared to the contralateral ear (Fig. 3).

In three patients, the contralateral healthy ear's saccule became larger than the utricle, with the confluence between these two compartments in one of these cases (two patients with grade I and one patient with grade II vestibular EH in Bernaerts scale). No cochlear endolymphatic hydrops was found in asymptomatic ears among analyzed patients.

3.3. Correlation between MRI classification of endolymphatic hydrops and clinical features

The endolymphatic space dilatation in MRI did not correlate with the duration of MD. Spearman's correlation test revealed that time from onset of the symptoms did not correlate with the advancement of the endolymphatic space dilatation neither in the cochlea ($p = 0.6500$) nor in the vestibule ($p = 0.2425$ and $p = 0.1817$ for Barath and Bernaerts scales, respectively) (Fig. 4 **panel I**). No correlation between the

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Table 3. Numerical table presenting number of patients with cochlear and vestibular endolymphatic hydrops assessed with the Barath and Bernaerts grading systems. CH – cochlear hydrops; VH – vestibular hydrops.

cochlear hydrops	vestibular hydrops Barath VH normal Bernaerts VH normal	Bernaerts VH grade I	Barath VH grade I Bernaerts VH grade II	Barath VH grade II Bernaerts VH grade III
Barath CH normal	3	4	0	0
Barath CH grade I	0	6	16	3
Barath CH grade II	0	1	5	0

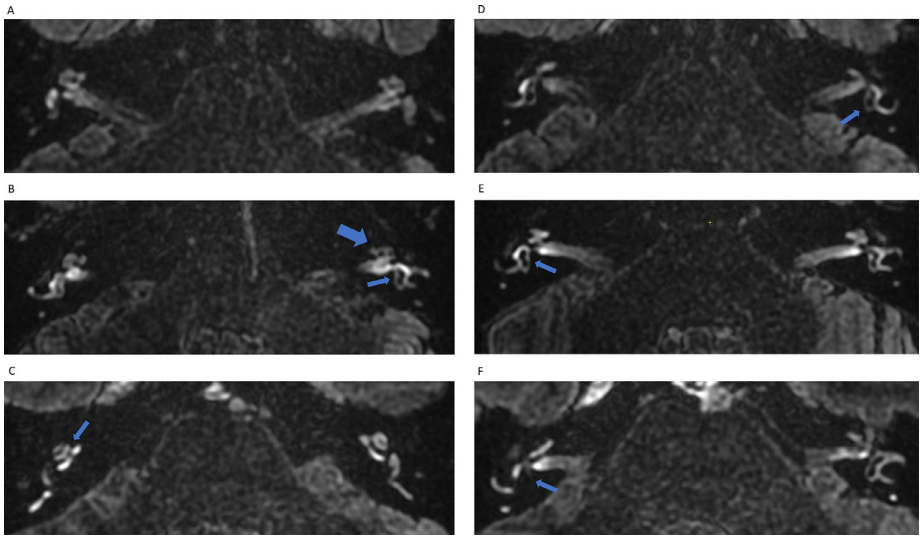

Fig. 2. Magnetic resonance imaging (MRI) example scans of patients with clinically defined Ménière's disease (MD). Affected ears are marked with arrows.
(A) An example case of the normal cochlea where scala vestibuli is evenly enhanced - a 37-year-old male with right-sided MD for the last 13 years, the hearing level within a normal range (PTA 20 dB HL), and SP/AP ratio 0.34;
(B) An example case of cochlear hydrops grade I - partial obstruction of the scala vestibuli by mildly dilated cochlear duct (pointed by the big arrow); An example case of vestibular hydrops grade II using Bernaerts modification (Barath grade I) - dilatation and confluence of saccule and utricle with visible circular enhancing perilymphatic space of vestibule (pointed by the small arrow) - a 54-year-old male with MD in the left ear for the last three years with PTA level 35 dB HL, and SP/AP ratio 0.22;
(C) An example case of cochlear hydrops grade II - distended cochlear duct entirely obliterating scala vestibuli (pointed by an arrow) - a 53-year-old male with MD on the right side for the last 21 years, PTA level 68.75 dB HL, and the SP/AP ratio 1.03;
(D) An example case of normal vestibule without hydrops - non-enhancing saccule and utricle are easily visible, and the saccule is smaller than the utricle (pointed by an arrow) - a 37-year-old male with right-sided MD for the last 13 years, PTA 20 dB HL, and SP/AP ratio 0.34;
(E) An example case of vestibular hydrops grade I using Bernaerts modification (Barath grade 0) - so-called extra low-grade vestibular hydrops, saccule is enlarged but still separated from the utricle (pointed by an arrow)) - a 60-year-old male with right-sided MD for the last year, PTA 32.5 dB HL, and SP/AP ratio 0.73;
(F) An example case of vestibular hydrops grade III using Bernaerts modification scale (Barath grade II) - in the vestibule, no perilymphatic space is visible due to saccule and utricle enlargement (pointed by an arrow) - a 58-year-old female with right-sided MD for the last five years, PTA level 67.55 dB HL, SP/AP ratio 0.47.

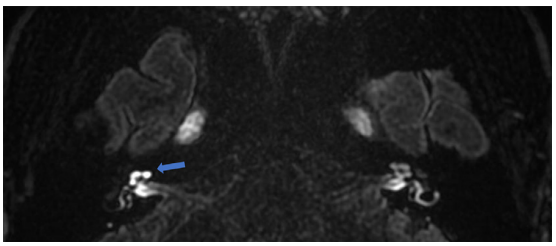

Fig. 3. Magnetic resonance imaging (MRI) example scan of a 69-year-old male with a clinical diagnosis of definite Ménière's disease in the right ear. The axial plane, delayed Gd-enhanced images did not show endolymphatic hydrops according to Barath and Bernaerts scales. However, perilymphatic enhancement is increased in the cochlea (pointed by an arrow) on the affected side compared to the contralateral normal inner ear, indicating impairment of the blood-perilymph barrier.

EH severity and the patient's age was found ($p = 0.9637$, $p = 0.7009$, and $p = 0.8552$, respectively).

There was no significant relationship between the average number of vertigo spells, self-estimated severity of tinnitus, aural fullness, or balance problems in the last six months, and EH degree, as shown by Spearman's correlation test ($p>0.05$) (Fig. 4 **panel II and III**). Analyzing the AAO-HNS functional level scale and the MRI results, no correlation was found ($p>0.05$). U-Mann-Whitney test revealed no statistically significant differences in the EH degrees between patients with and without Tumarkin attacks in their past medical history ($p = 0.5752$, $p = 0.5150$, and $p = 0.8193$, respectively for Barath cochlear and vestibular scales, and Bernaerts scale).

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3.4. Correlation between MRI classification of endolymphatic hydrops and audiovestibular test results

A statistically significant correlation was found between the PTA level and the vestibular EH degree in the Bernaerts scale in the affected ears ($p = 0.0327$). However, Spearman's correlation test revealed no statistically significant relationship when used the Barath system ($p = 0.0726$). Evaluating vestibular EH assessed using the Barath scale, EH degree correlated with the hearing level at the frequency of 2000 Hz only ($p = 0.04820$), while vestibular EH assessed with the Bernaerts grading system correlated with hearing loss at individual audiometric frequencies of 250 Hz and 2000 Hz ($p = 0.0218$ and $p = 0.0441$ respectively. However, there was no correlation between the cochlear EH degree and the PTA level ($p = 0.9801$). Moreover, no correlation was found between each of the individual frequencies hearing thresholds and the cochlear EH ($p>0.05$) (Fig. 4 **panel IV**).

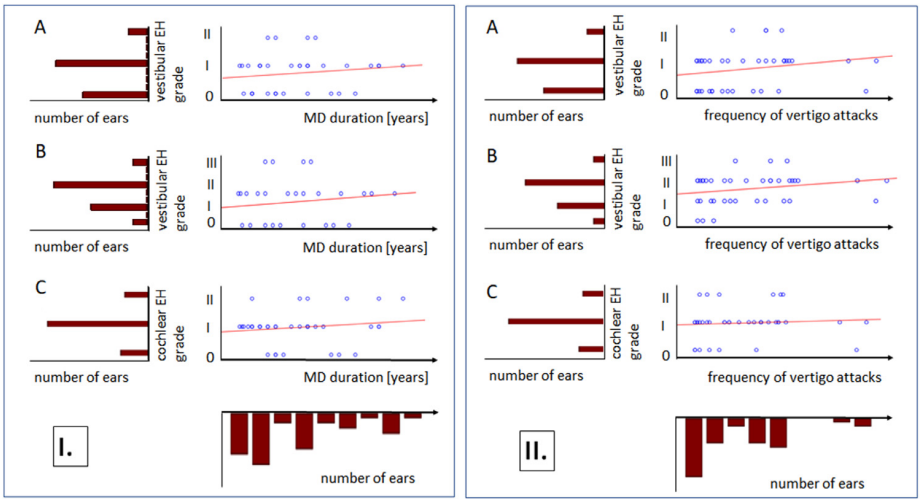

Fig. 4. Panel I. The correlation between the Ménière's disease (MD) duration and the endolymphatic hydrops (EH).
(A) Correlation between the MD duration and the vestibular EH assessed with the Barath scale (Spearman's correlation test, statistical significance p=0.2425)
(B) Correlation between the MD duration and the vestibular EH assessed with the Beraerts scale (Spearman's correlation test, statistical significance p=0.1817)
(C) Correlation between the MD duration and the cochlear EH assessed with the Barath scale (Spearman's correlation test, statistical significance p=0.6500)
Panel II. The correlation between the average number of vertigo spells in the last six months and the endolymphatic hydrops (EH).
(A) Correlation between the MD duration and the vestibular EH assessed with the Barath scale (Spearman's correlation test, statistical significance p= 0.0852)
(B) Correlation between the MD duration and the vestibular EH assessed with the Bernaerts scale (Spearman's correlation test, statistical significance p= 0.1113)
(C) Correlation between the MD duration and the cochlear EH assessed with the Barath scale (Spearman's correlation test, statistical significance p= 0.2372)
Panel III. The correlation between the average level of balance problems in the last six months self-evaluated with 0-6 Arenberg scale and the endolymphatic hydrops (EH).
(A) Correlation between the balance problems and the vestibular EH assessed with the Barath scale (Spearman's correlation test, statistical significance p=0.3358)
(B) Correlation between the balance problems and the vestibular EH assessed with the Bernaerts scale (Spearman's correlation test, statistical significance p=0.1783)
(C) Correlation between the balance problems and the cochlear EH assessed with the Barath scale (Spearman's correlation test, statistical significance p=0.2932)
Panel IV. The correlation between the hearing level and the endolymphatic hydrops (EH).
(A) Correlation between the pure tone average (PTA) and the vestibular EH assessed with the Barath scale (Spearman's correlation test, statistical significance p=0.0726)
(B) Correlation between the pure tone average (PTA) and the vestibular EH assessed with the Bernaerts scale (Spearman's correlation test, statistical significance p=0.0327)
(C) Correlation between the pure tone average (PTA) and the cochlear EH assessed with the Barath scale (Spearman's correlation test, statistical significance p=0.9801)
Panel V. The correlation between the transtympanic electrocochleography results – summating potential to action potential ratio (SP/AP) and the endolymphatic hydrops (EH).
(A) Correlation between the SP/AP ratio and the vestibular EH assessed with the Barath scale (Spearman's correlation test, statistical significance p= 0.0874)
(B) Correlation between the SP/AP ratio and the vestibular EH assessed with the Bernaerts scale (Spearman's correlation test, statistical significance p= 0.0354)
(C) Correlation between the SP/AP ratio and the cochlear EH assessed with the Barath scale (Spearman's correlation test, statistical significance p= 0.9223)
Panel VI. The correlation between the caloric responses in the VNG test and the endolymphatic hydrops (EH).
(A) Correlation between the caloric responses and the vestibular EH assessed with the Barath scale (Spearman's correlation test, statistical significance $p = 0.0410$)
(B) Correlation between the caloric responses and the vestibular EH assessed with the Bernaerts scale (Spearman's correlation test, statistical significance $p = 0.0883$)
(C) Correlation between the caloric responses and the cochlear EH assessed with the Barath scale (Spearman's correlation test, statistical significance p= 0.3317)

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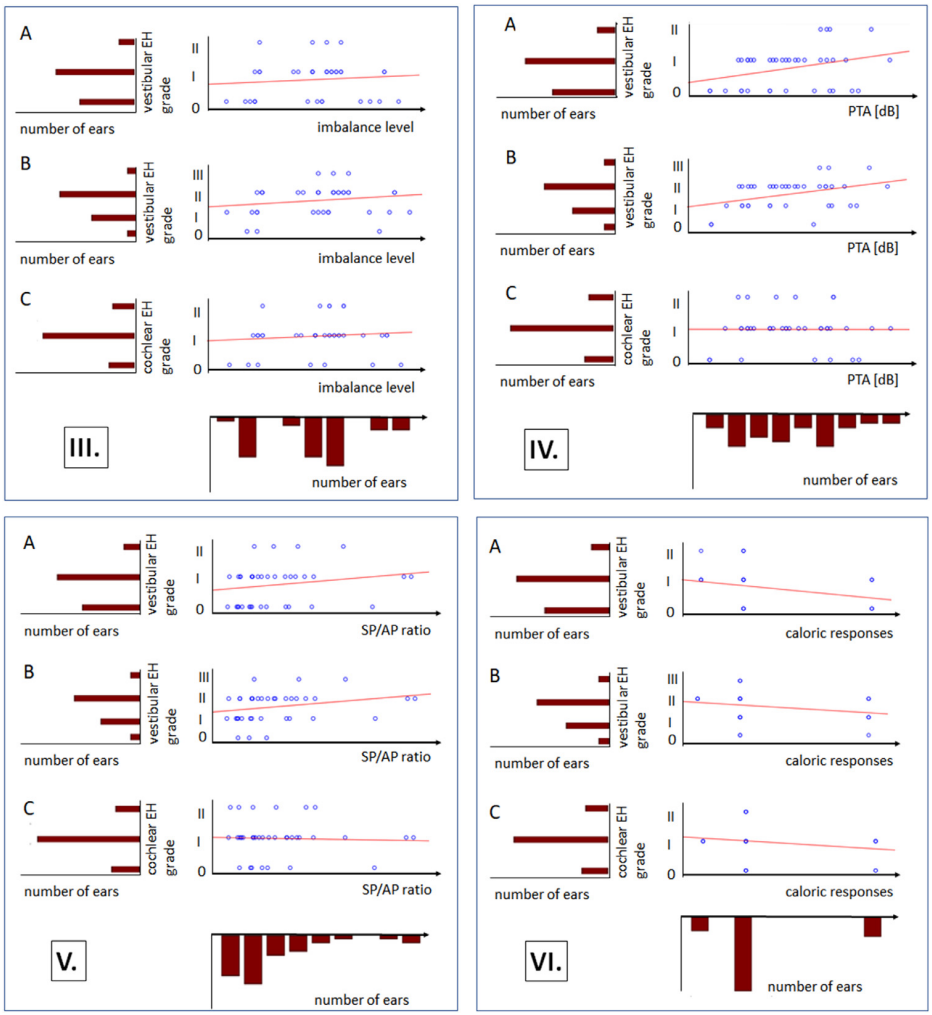

Fig. 4. Continued

Among patients with a cochlear hearing loss pattern in ABR, 66.67% had grade I, and 26.67% had grade II cochlear EH on the Barath scale, while only 6.67% (1 patient) had no cochlear hydrops. However, 100% of patients with a complete absence of auditory responses had no hydrops in the cochlea, while all patients with non-cochlear hearing loss pattern had grade I cochlear EH. In subpopulation with normal auditory responses, 33.33% had no hydrops, 50.00% had grade I, and 16.67% had grade II cochlear EH. Taken together, 45.16% of the affected ears with cochlear EH had a cochlear hearing loss pattern of ABR result, while the rest had normal auditory responses or non-cochlear hearing loss.

In patients with cochlear hearing loss in ABR, 80% of the affected ears had vestibular EH in the Barath grading scale, while using Bernaerts modification, EH in the vestibule was found in 100% of them. In contrast, the relationship between the cochlear EH and the ABR results was not observed. Patients with the complete absence of auditory response presented no vestibular hydrops features in MRI analyzing scans with the Barath scale.

Among ears with normal ABR results, 66.67% had no EH in the vestibule using the Barath grading system. According to the Bernaerts scale, the saccule was larger than the utricle in 6 of these ears. A normal vestibule was observed in 16.67%.

In TT-EChoG, the SP/AP ratio correlated neither with the vestibular nor the cochlear EH degree in the Barath's scale, as revealed by Spearman's correlation test. In contrast, using modification proposed by Bernaerts significant positive correlation was found between the vestibular EH grade and SP/AP ratio ($p = 0.0354$) (Fig. 4-**V**).

The relationship between the stage of the EH and horizontal semicircular canal function evaluated with VNG was assessed (Fig. 4-**VI**). A weak but significant negative correlation was found only evaluating vestibular EH with the Barath scale ($p = 0.0410$). Using the Barath grading system, 62.5% of the ears with vestibular EH presented vestibular weakness, while 20.83% had no caloric responses, 12.5% had normal caloric responses, and 2.63% (one patient) had central vestibular dysfunction. However, 37.5% of ears with weaker caloric responses had no hydrops in the vestibule, while it was found in 100% of ears

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with complete vestibular paresis. According to Barath and Bernaerts grading scales, 42.86% and 85.71% of patients with normal caloric responses had vestibular EH in MRI, respectively.

Among patients with cochlear EH, 61.29% presented weaker caloric responses in VNG, 16.13% normal caloric responses, 16.13% vestibular paresis, and 6.45% (two patients) central vestibular dysfunction.

4. Discussion

In the study performed by Barath et al. [8], 90% of clinically affected ears presented EH in MRI and considered patients with definite MD only, 95%. Bernaerts et al. [9] proposed modification of the vestibular EH evaluating system adding an extra-low grade of the vestibular EH based on the saccular enlargement. In our study, Bernaerts modification was found to be meaningful, as the sensitivity of MRI increased from 81.6% (using Barath scale) to 92,1% (with Bernaerts modification), considering dilatation of the endolymphatic space in one part of the inner ear (the cochlea or the vestibule) sufficient to recognize EH. Recently, many studies are focused on the saccular endolymphatic space dilatation. In 2017 Attye et al. [11] described saccular-morphology-based classification evaluating an inversion of saccule to utricle volume ratio (SURI) in a sagittal MRI slice. An abnormal SURI >=1 was found in half of the patients with clinically diagnosed MD, while among the control group, no one had the saccule larger than the utricle. Kahn et al. [17] evaluated endolymphatic space dilatation in the cochlea, saccule, utricle, and semicircular canal ampullas separately proposed a compartmental, anatomically based EH classification. They found EH in the cochlea in 88%, whereas the saccular EH in 91% of the symptomatic ears. Utricular and ampullar hydrops were found in 45% and 8.5% of the clinically affected ears, respectively. Interestingly, dilatation of the saccular endolymphatic space was associated with cochlear EH in 97%, except for one patient with isolated saccular EH, while the utricle and the ampullae were involved only in patients with severe cochlear and saccular EH.

In our study, analyzing MRI scans with the Barath grading system, vestibular EH was found only among patients with developed cochlear EH. It is consistent with the theory of continuous hydrops progression involving the cochlear duct first and then the vestibular endolymphatic space [25,26]. However, considering Bernaerts modification, enlargement of the saccule without the cochlear duct dilatation was found in 4 patients (10.53% of affected ears) as the only EH sign. Morita et al. [27] analyzed 3D images of the inner ear reconstructed from temporal bone sections and implied that the saccule has higher mechanical compliance than the utricle; hence it is more sensitive than distension caused by the EH [28]. Kahn et al. [17] hypothesized that the endolymphatic space's continuous extension in following inner ear compartments results from the endolymphatic volume regulation failure. It is known that dark cells producing endolymph are mainly localized in the cochlear duct, the utricle, and the ampullas, with a low concentration in the saccule [29]. Bast's valve prevents endolymphatic backflow from the utricle; the cochlea's endolymph probably causes the saccular hydrops. Therefore, dilatation of the saccule may be crucial in the early stages of MD, when it can act as a reservoir of the endolymph due to its direct proximity to the cochlear duct.

Yoshida et al. [30] proposed the vestibular EH as a specific MD predictor since it rarely occurs in the control population. In contrast, dilatation of the endolymphatic space in the cochlea, especially apical turn, was commonly found in healthy control ears. One can presume that the EH progression from the cochlear duct to the vestibule may be correlated with the appearance of MD symptoms. The saccule is the first compartment of the vestibule affected by the EH and should be evaluated very carefully while analyzing the MRI.

Recently, increased permeability of the blood-perilymph barrier is suspected of playing a role in MD pathogenesis. Bernaerts et al. [9] added evaluation of the perilymph enhancement comparing the affected ear to the contralateral side to obtain higher specificity.

In our study, asymmetrical perilymph enhancement was found only in one ear. Interestingly, it occurred in a patient without EH, with normal hearing level and TT-ECoG result, suggesting that blood-perilymph barrier impairment plays an essential role during MD's early stages.

The goal of our study was to evaluate possible associations between the Barath [8] and recently proposed Bernaerts [9] classification systems and clinical and audiovestibular performance. There has been still a debate to what degree the MRI findings are associated with the clinical and audiovestibular test results.

In our study, EH severity specified with the use of MRI scans, according to both the Barath grading system and the Bernaerts grading system, did not correlate with the disease duration counted from the first symptom onset (vertigo, tinnitus, aural fullness, and hearing loss. It is in agreement with previous studies evaluating EH with different semi-quantitative grading systems [17,30,31]. Bernaerts et al. [9] found a significant correlation between the MD duration and the endolymphatic space dilatation. We presume that different results among these studies are determined on heterogeneous patients population as the natural history of MD is characterized by unpredictable fluctuations and spontaneous remissions. It is unsure whether the disease duration was counted from the first symptom onset or the complete clinical picture.

EH is thought to be a dynamic phenomenon. As reported in several studies, in a single patient, the endolymphatic space volume differs between repeated MRI reflecting the MD's fluctuating course [32,33]. In our study, the correlation between the MRI's EH degree and the severity of MD symptoms was investigated. Interestingly, no correlation between the intensity of tinnitus, aural fullness, or balance problems and endolymphatic hydrops was found, which may indicate other than endolymphatic space dilatation causes of these symptoms as suggested by Merchant et al. [34]. However, in our study, the questionnaire was filled-out retrospectively, and patients may be, to a certain extend, inaccurate in self-evaluating their complaints intensity over the last six months. Future study is

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needed with a survey given an adequate period before MRI examination to verify a relationship between current symptoms severity and EH degree.

Since the improvement of a patient's quality of life is a fundamental goal of MD treatment, the relationship between self-estimated functional level and EH degree was analyzed in our study. EH assessed with both scales, the Barath and Bernaerts, neither cochlear nor vestibular EH degree correlated with patients' functional level. Endolymphatic volume was found to be not the sole factor affecting the quality of life in MD. Nevertheless, future studies investigating both the volume and the function of the cochlea and vestibule compartments are needed.

In our study, in contrast to Kanh et al. [17], there was no significant difference in EH severity between patients with and without Tumarkin attacks in the past medical history. In our study, patients' subpopulation with the Tumarkin crisis is heterogeneous, with disease duration from 3 to 18 years and PTA level from 32,5 to 67,5 dB. As drop attacks in MD are thought to be a consequence of the otolith organ's instability, it may be speculated that detaching of the saccular otoconia may occur in the early MD stage with slightly dilated endolymphatic space as well as in the labyrinth with severe hydrops.

Correlation between the EH and the hearing loss level has been found in many studies performed recently [13,15,17,31,35,36]. In our study, the PTA level correlated with the severity of vestibular EH evaluated in the Bernaerts grading system. Moreover, two patients with normal inner ear MRI had normal hearing levels. In a recent study, Sluydts et al. [36] investigated the relationship between the Bernaerts grading scale and audiovestibular test results. They found PTA level significantly higher in ears with vestibular EH grade III than the ears without vestibular hydrops, which is consistent with our results. In contrast to most studies found in literature, they found no significant differences in the PTA level between ears with cochlear hydrops grade I and II. However, a low-frequency PTA differed between these two groups of patients. In our study, the cochlear EH degree did not correlate with the PTA level nor with each of the frequencies examined.

It has to be mentioned that the PTA level correlated with patients' age also, with the strongest correlation with the frequency of 4000 Hz. The pure tone hearing levels differed significantly between the affected and the normal contralateral ear, so we consider the hearing loss in the symptomatic ears due to MD and not only the presbyacusis.

Determination of the relationship between the EH degree and hearing loss is essential. The severity of the MD is clinically estimated depending on the hearing level, and tone audiometry remains the only objective test used in MD diagnosis according to AAO-HNS Guidelines [4,5]. Moreover, abnormal hearing thresholds were found in guinea pigs with induced hydrops of the inner ear [29,37].

Patients with MD suffer from fluctuating hearing loss, with remissions characterized by normal hearing during the disease's early stages. In the present study, the PTA level correlated with the vestibular EH degree according to the Bernaerts scale; this phenomenon may also apply to the fluctuating endolymphatic space volume in the saccule.

As we hypothesized in our study, the most numerous patients group had cochlear hearing loss, and the majority of them had cochlear and vestibular EH confirmed in MRI scans. However, patients with the complete absence of auditory responses had no hydrops in the cochlea or the vestibule. Surprisingly, the majority of the patients with normal ABR results had cochlear and vestibular EH. To our best knowledge, there are no previous studies in the literature that analyzed the correlation between MRI and ABR results in patients with MD. In our study, cochlear EH was found in 93.33% of ears with cochlear hearing loss in ABR. We believe this coincidence may be potentially meaningful; however, there is no statistically significant correlation between the ABR result pattern and the hydrops severity. We presume cochlear and non-cochlear hearing loss in MD may occur under other than endolymphatic space dilatation cause.

In our study, taking into account TT-ECochG results, no correlation between the SP/AP ratio and the cochlear or vestibular EH degree using the Barath grading system was found. Interestingly, evaluating MR images with the four-grade scale modified by Bernaerts, vestibular EH correlated with the SP/AP ratio. The relationship between the ECochG results and the EH degree was investigated by Yamamoto et al. [38], who performed trans-tympanic EChoG (TT-ECochG) and MRI in a heterogeneous patients population with MD, delayed EH, and fluctuating hearing loss without vertigo. They found the SP/AP ratio higher in patients with significant vestibular EH compared to groups with mild and none hydrops in the vestibule; however, differences were not statistically significant. The ECochG results in the patients with significant cochlear EH differed from the subpopulations with mild and none cochlear EH. No significant differences were found between groups without EH and with mild EH in the cochlea. Seo et al. [13] divided patients with definite MD into two groups with visualized and non-visualized cochlear hydrops and found significant differences in TT-ECochG results between these subpopulations.

In our study, vestibular EH was assessed with the Barath scale and, more precisely, using the four-grade Bernaerts scale. The correlation with the SP/AP was found, suggesting that dilatation of the saccular endolymphatic space impacts the electrical potentials generated in the cochlea. Interestingly, in two patients without EH, SP/AP ratio was > 0.33 despite the normal hearing level. Thus, in the early stages of MD without irreversible hearing loss, TT-ECoG abnormalities may occur without EH developed.

In the present study, no correlation between the cochlear EH degree and the caloric responses in VNG was found, consistent with previous studies found in the literature [31]. On the other hand, using the Barath scale, a significant correlation between the vestibular EH and the canal paresis in VNG was found. Cho et al. [39] found a correlation between the canal paresis and the relative vestibule ratio in MRI. Interestingly, in caloric tests, the canal paresis value was significantly worse in patients with the horizontal semicircular canal hydrops. In our study, hydrops of the horizontal semicircular canal was

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not evaluated separately. However, a relationship between the VNG results and vestibular hydrops degree was found only using the Barath scale. It may indicate an essential role of utricular endolymphatic space dilatation in the canal paresis caused by their anatomical conditions, direct proximity to the semicircular canal. The endolymph of the utricle may interfere with the canal's responses and functioning, causing a deterioration of the VNG response. Moreover, our results suggest the compartmental character of the vestibular dysfunction in MD.

Several studies investigated the relationship between the MRI and the vestibular function assessed with vestibular evoked myogenic potentials (VEMPs) [15,17]. Thus, the correlation between the vestibular EH and the VEMPs responses would be helpful to understand the relationship between the endolymphatic space dilatation and the loss of function affecting particular compartments of the vestibule.

5. Conclusions

Many attempts have been made to establish a reliable diagnostic test for MD, as the clinical course is individually variable, leading to a delay in diagnosis. Several semi-quantitative grading systems for EH assessment in MRI have been commonly used, but none of them have been included in the international diagnostic guidelines yet. In our study, two similar MRI grading systems were used; however, several differences were found compared to one another. The Bernaerts scale was found to be significantly more sensitive than the Barath scale, and several relationships between the radiological and clinical data were found. Therefore, several MRI evaluating scales and correlating them with the clinical features are needed to establish the so-called gold standard in MD diagnostic. The increased perilymphatic enhancement of the cochlea and an extra low-grade vestibular hydrops distinguished in the Bernaerts scale may increase MD diagnosis sensitivity. Magnetic resonance findings in MD support the clinical diagnosis and may help to understand MD pathophysiology better. This study adds to the knowledge and diagnostics in MD for healthcare to improve patients' treatment.

Disclosure Statement

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Wnioski

Badanie MR ucha wewnętrznego pozwala na przyżyciowe potwierdzenie obecności wodniaka śródchłonki u pacjentów z objawami choroby Ménière'a. Na postawie przeprowadzonych badań wykazano istotne statystyczne różnice w czułości wykrywania wodniaka śródchłonki w MR pomiędzy skalą zaproponowaną przez Barath i wsp. oraz jej modyfikacją wprowadzoną przez Bernaerts i wsp. Wyniki pozwalają stwierdzić, że powiększenie woreczka oraz asymetryczne wysycenie kontrastem ucha wewnętrznego, stosowane w drugiej ze skal, są istotnymi cechami radiologicznymi wodniaka śródchłonki i pozwalają na zwiększenie czułości badania MRI w ocenie ucha wewnętrznego u pacjentów z chorobą Ménière'a.

Na podstawie przeprowadzonych badań własnych można zaobserwować, że wodniak przedsionka obejmujący łagiewkę występował jedynie u pacjentów z poszerzonym przewodem ślimaka oraz powiększeniem woreczka. Potwierdza to teorię rozwoju choroby Ménière'a, w myśl której nadmiar endolimfy gromadzi się początkowo w przewodzie ślimaka, a następnie wodniak obejmuje kolejno woreczek i łagiewkę.

W badaniach stwierdzono także, że zaawansowanie wodniaka endolimfatycznego koreluje z poziomem niedosłuchu w audiometrii tonalnej, która według wytycznych Amerykańskiej Akademii Otorynolaryngologii, Chirurgii Głowy i Szyi (ang. *American Academy of Otorhinolaryngology, Head and Neck Surgery*, AAO-HNS) pozostaje nadal badaniem wymaganym do rozpoznania choroby Ménière'a. Istotny związek z zaawansowaniem wodniaka przedsionka wykazywał także stosunek amplitudy potencjału sumacyjnego do amplitudy potencjału czynnościowego (SP/AP) w badaniu elektrokochleografii transtympanalnej (TT-ECochG). Wykazane korelacje dowodzą wpływu poszerzenia przestrzeni endolimfatycznych na uszkodzenie słuchu w chorobie Ménière'a.

W przedstawionych badaniach własnych stopnień zaawansowania wodniaka śródchłonki nie wykazywał istotnych korelacji z czasem trwania choroby, co można tłumaczyć zmiennym osobniczo, nieprzewidywalnym przebiegiem schorzenia. Nie wykazano także istotnych statystycznie korelacji pomiędzy zaawansowaniem wodniaka w MR a subiektywnym nasileniem objawów choroby. Należy jednak mieć na uwadze, że pacjenci wypełniali ankietę dotyczącą głównych dolegliwości retrospektywnie, co mogło wpłynąć na dokładność podanych danych. Ponadto, brak istotnych statystycznie korelacji pomiędzy zaawansowaniem wodniaka w MRI a obrazem klinicznym jest opisywany w literaturze i może być spowodowany złożonym podłożem dolegliwości w chorobie Ménière'a, na które poza poszerzeniem przestrzeni endolimfatycznych mogą składać się także inne niepoznane dotąd czynniki.

Ocena wodniaka śródchłonki w badaniu MR jest zagadnieniem stosunkowo nowym na świecie i jeszcze nie poruszanym w naszym kraju. Prezentowane prace stanowiące moją rozprawę doktorską są pierwszymi w naszym kraju dotyczącymi omawianej tematyki. Zaprezentowane w monotematycznym cyklu artykułów badania dowodzą, że MR jest cennym badaniem w diagnostyce choroby Ménière'a i stwarza możliwość potwierdzenia obecności wodniaka śródchłonki za życia pacjenta. Poznanie korelacji pomiędzy zaawansowaniem choroby w badaniu obrazowym a obrazem klinicznym i wynikami badań audiologicznych i otoneurologicznych jest kluczowe w procesie zrozumienia patogenezy choroby Ménière'a. Przedstawiony cykl prac stanowiących moją rozprawę doktorską przyczynia się do poszerzenia wiedzy dotyczącej choroby Ménière'a.

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Komisja Bioetyczna przy Warszawskim Uniwersytecie Medycznym
w dniu 10 czerwca 2019 r. po zapoznaniu się z wnioskiem:

Lek.med. Emilia Wnuk,
II Zakład Radiologii Klinicznej,
ul. Banacha 1a, 02-097 Warszawa

dotyczącym: wyrażenia opinii w sprawie badania pt : „ Ocena układu przedsionkowo-ślimakowego metodą rezonansu magnetyczneo u pacjentów z podejrzeniem choroby Meniera."

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1. ***Jasińska A***, *Lachowska M, Wnuk E, Niemczyk K. Magnetic resonance imaging of the inner ear in the diagnostics of Ménière's disease. Otorynolaryng Pol 2021:75(2):1-8. doi: 10.5604/01.3001.0014.6176*

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2. ***Jasińska A***, *Wnuk E, Pierchała K, Niemczyk K. Wodniak śródchłonki potwierdzony przy użyciu 3-teslowego skanera MR u pacjentów z obrazem klinicznym choroby Ménière'a. Polski Przegląd Otorynolaryngologiczny 2019;8(3):20-23.*

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3. ***Jasińska A***, *Lachowska M, Wnuk E, Pierchała K, Rowiński O, Niemczyk K. Correlation between magnetic resonance imaging classification of endolymphatic hydrops and clinical manifestations and audiovestibular test results in patients with definite Ménière's disease. Auris Nasus Larynx, Online ahead of print doi: 10.1016/j.anl.2021.03.027*

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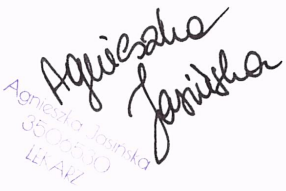

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1. *Jasińska A, Lachowska M, Wnuk E, Niemczyk K. Magnetic resonance imaging of the inner ear in the diagnostics of Ménière's disease. Otorynolaryng Pol 2021:75(2):1-8. doi: 10.5604/01.3001.0014.6176*

   Szacowany wkład w publikację – 16 %

2. *Jasińska A, Lachowska M, Wnuk E, Pierchała K, Rowiński O, Niemczyk K. Correlation between magnetic resonance imaging classification of endolymphatic hydrops and clinical manifestations and audiovestibular test results in patients with definite Ménière's disease. Auris Nasus Larynx, Online ahead of print doi: 10.1016/j.anl.2021.03.027*

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1. *Jasińska A, Lachowska M, Wnuk E, Niemczyk K. Magnetic resonance imaging of the inner ear in the diagnostics of Ménière's disease. Otorynolaryng Pol 2021:75(2):1-8. doi: 10.5604/01.3001.0014.6176*

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2. *Jasińska A, Wnuk E, Pierchała K, Niemczyk K. Wodniak śródchłonki potwierdzony przy użyciu 3-teslowego skanera MR u pacjentów z obrazem klinicznym choroby Ménière'a. Polski Przegląd Otorynolaryngologiczny 2019;8(3):20-23.*

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3. *Jasińska A, Lachowska M, Wnuk E, Pierchała K, Rowiński O, Niemczyk K. Correlation between magnetic resonance imaging classification of endolymphatic hydrops and clinical manifestations and audiovestibular test results in patients with definite Ménière's disease. Auris Nasus Larynx, Online ahead of print doi: 10.1016/j.anl.2021.03.027*

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1. *Jasińska A, Wnuk E, Pierchała K, Niemczyk K. Wodniak śródchłonki potwierdzony przy użyciu 3-teslowego skanera MR u pacjentów z obrazem klinicznym choroby Ménière'a. Polski Przegląd Otorynolaryngologiczny 2019;8(3):20-23.*

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2. *Jasińska A, Lachowska M, Wnuk E, Pierchała K, Rowiński O, Niemczyk K. Correlation between magnetic resonance imaging classification of endolymphatic hydrops and clinical manifestations and audiovestibular test results in patients with definite Ménière's disease. Auris Nasus Larynx, Online ahead of print doi: 10.1016/j.anl.2021.03.027*

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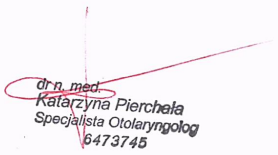

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1. *Jasińska A, Lachowska M, Wnuk E, Pierchała K, Rowiński O, Niemczyk K. Correlation between magnetic resonance imaging classification of endolymphatic hydrops and clinical manifestations and audiovestibular test results in patients with definite Ménière's disease. Auris Nasus Larynx, Online ahead of print doi: 10.1016/j.anl.2021.03.027*

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1. *Jasińska A, Lachowska M, Wnuk E, Niemczyk K. Magnetic resonance imaging of the inner ear in the diagnostics of Ménière's disease. Otorynolaryng Pol 2021:75(2):1-8. doi: 10.5604/01.3001.0014.6176*

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2. *Jasińska A, Wnuk E, Pierchała K, Niemczyk K. Wodniak śródchłonki potwierdzony przy użyciu 3-teslowego skanera MR u pacjentów z obrazem klinicznym choroby Ménière'a. Polski Przegląd Otorynolaryngologiczny 2019;8(3):20-23.*

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